

Barb  
only please

94606

Access DB#

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Dwayne C. Jones Examiner #: 731299 Date: 21 MAY 83  
Art Unit: 1614 Phone Number 30 8-4634 Serial Number: 071 718,290  
Mail Box and Bldg/Room Location: 2007, CML Results Format Preferred (circle): PAPER DISK E-MAIL  
2005, CML

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: \_\_\_\_\_

Inventors (please provide full names): Michael Wyllie

Earliest Priority Filing Date: 09 FEB 2000

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search claim 1, 4, 7  
and the method claim of 29

## STAFF USE ONLY

Searcher: 16-03

Searcher Phone #: \_\_\_\_\_

Searcher Location: \_\_\_\_\_

Date Searcher Picked Up: \_\_\_\_\_

Date Completed: 6-4-03

Searcher Prep & Review Time: 20

Clerical Prep Time: \_\_\_\_\_

Online Time: 76

## Type of Search

NA Sequence (#) \_\_\_\_\_

AA Sequence (#) \_\_\_\_\_

Structure (#) \_\_\_\_\_

Bibliographic \_\_\_\_\_

Litigation \_\_\_\_\_

Fulltext \_\_\_\_\_

Patent Family \_\_\_\_\_

Other \_\_\_\_\_

## Vendors and cost where applicable

STN 32-9

Dialog \_\_\_\_\_

Questel/Orbit \_\_\_\_\_

Dr. Link \_\_\_\_\_

Lexis/Nexis \_\_\_\_\_

Sequence Systems \_\_\_\_\_

WWW/Internet \_\_\_\_\_

Other (specify) \_\_\_\_\_

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# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 94606

TO: Dwayne C Jones  
Location: mail 2D01; room 2D07  
Art Unit: 1614  
Wednesday, June 04, 2003

Case Serial Number: 778290

From: Barb O'Bryen  
Location: Biotech-Chem Library  
CM1-6A05  
Phone: 308-4291 *POB*

barbara.obryen@uspto.gov

### Search Notes

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# STIC SEARCH RESULTS FEEDBACK FORM

## Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher or contact*:

Mary Hale, Information Branch Supervisor  
308-4258, CM1-1E01

## Voluntary Results Feedback Form

➤ I am an examiner in Workgroup:  Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature  
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library CM1 - Circ. Desk



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=> e ADRENERGIC ALPHA-ANTAGONISTS+all/ct

E1	0	BT6	D Chemicals and Drugs/CT
E2	0	BT5	Chemical Actions and Uses/CT
E3	0	BT4	Chemical Actions/CT
E4	0	BT5	D Chemicals and Drugs/CT
E5	0	BT4	Neurotransmitters and Neurotransmitter Agents/CT
E6	66	BT3	Neurotransmitter Agents/CT
E7	723	BT2	Adrenergic Agents/CT
E8	442	BT1	Adrenergic Antagonists/CT
E9	10288	-->	Adrenergic alpha-Antagonists/CT
E10	10288	MN	D14.100.50.200.100./CT
E11	10288	MN	D27.505.583.50.200.100./CT
		DC	an INDEX MEDICUS major descriptor
		NOTE	Drugs that bind to but do not activate alpha-adrenergic receptors thereby blocking the actions of endogenous or exogenous adrenergic agonists. Adrenergic alpha-antagonists are used in the treatment of hypertension, vasospasm, peripheral vascular disease, shock, and pheochromocytoma.
		INDX	GEN or unspecified; prefer specifics; do not confuse with ADRENERGIC ALPHA-AGONISTS; DF: ADREN ALPHA ANTAG
		AQ	AD AE AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
		PNTE	Sympatholytics (1966-1968)
		HNTE	95; was ADRENERGIC ALPHA RECEPTOR BLOCKADERS 1969-94 (Prov 1969-72)
		ONTE	use ADRENERGIC ALPHA-ANTAGONISTS to search ADRENERGIC ALPHA RECEPTOR BLOCKADERS 1969-94 (as Prov 1969-72)
		MHTH	NLM (1969)
E12	0	UF	ADREN ALPHA ANTAG/CT
E13	0	UF	Adrenergic alpha Antagonists/CT
E14	0	UF	Adrenergic alpha Blockers/CT
E15	0	UF	Adrenergic alpha Receptor Blockaders/CT
E16	0	UF	Adrenergic alpha-Blockers/CT
E17	0	UF	Adrenergic alpha-Receptor Blockaders/CT
E18	0	UF	Agents, alpha-Adrenergic Blocking/CT
E19	0	UF	Blockaders, Adrenergic alpha-Receptor/CT
E20	0	UF	Blockaders, alpha-Adrenergic Receptor/CT
E21	0	UF	Blockers, alpha-Adrenergic/CT
E22	0	UF	Blocking Agents, alpha-Adrenergic/CT
E23	0	UF	Receptor Blockaders, alpha-Adrenergic/CT
E24	0	UF	alpha Adrenergic Blockers/CT
E25	0	UF	alpha Adrenergic Blocking Agents/CT
E26	0	UF	alpha Adrenergic Receptor Blockaders/CT
E27	0	UF	alpha Blockers, Adrenergic/CT
E28	0	UF	alpha-Adrenergic Blockers/CT
E29	0	UF	alpha-Adrenergic Blocking Agents/CT
E30	0	UF	alpha-Adrenergic Receptor Blockaders/CT
E31	0	UF	alpha-Antagonists, Adrenergic/CT
E32	0	UF	alpha-Blockers, Adrenergic/CT
E33	0	UF	alpha-Receptor Blockaders, Adrenergic/CT
E34	439	NT1	Dibenamine/CT
E35	954	NT1	Dihydroergotoxine/CT
E36	512	NT2	Ergoloid Mesylates/CT
E37	645	NT1	Doxazosin/CT
E38	512	NT1	Ergoloid Mesylates/CT
E39	1131	NT1	Idazoxan/CT
E40	202	NT1	Indoramin/CT

} *α adrenergic antagonists according to Medline*

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E41	1474	NT1	Labetalol/CT
E42	1428	NT1	Mianserin/CT
E43	265	NT1	Moxisylyte/CT
E44	296	NT1	Nicergoline/CT
E45	4513	NT1	Phenoxybenzamine/CT
E46	8184	NT1	Phentolamine/CT
E47	150	NT1	Piperoxan/CT
E48	6270	NT1	Prazosin/CT
E49	645	NT2	Doxazosin/CT
E50	4551	NT1	Quinidine/CT
E51	816	NT1	Tolazoline/CT
E52	4528	NT1	Yohimbine/CT
*****	END***		



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=> e e3l+all

E1	0	BT6	D Chemicals and Drugs/CT
E2	0	BT5	Chemical Actions and Uses/CT
E3	0	BT4	Chemical Actions/CT
E4	0	BT5	D Chemicals and Drugs/CT
E5	0	BT4	Neurotransmitters and Neurotransmitter Agents/CT
E6	66	BT3	Neurotransmitter Agents/CT
E7	802	BT2	Cholinergic Agents/CT
E8	1379	BT1	Cholinergic Antagonists/CT
E9	3097	-->	Muscarinic Antagonists/CT
E10	3097	MN	D14.100.120.200.500./CT
E11	3097	MN	D27.505.583.120.200.500./CT
		DC	an INDEX MEDICUS major descriptor
		NOTE	Drugs that bind to but do not activate muscarinic cholinergic receptors (RECEPTORS, MUSCARINIC), thereby blocking the actions of endogenous acetylcholine or exogenous agonists. Muscarinic antagonists have widespread effects including actions on the iris and ciliary muscle of the eye, the heart and blood vessels, secretions of the respiratory tract, GI system, and salivary glands, GI motility, urinary bladder tone, and the central nervous system. Antagonists that discriminate among the various muscarinic receptor subtypes and might allow better control of peripheral and central actions are under development.
		INDX	GEN or unspecified; prefer specifics; DF: MUSCARINIC ANTAG
		AQ	AD AE AN BL CF CH CL CS CT DU EC HI IM IP ME PD PK PO RE SD ST TO TU UR
		PNTE	Parasympatholytics (1966-1994)
		HNTE	95; ANTIMUSCARINIC AGENTS was see PARASYMPATHOLYTICS 1969-94
		ONTE	use PARASYMPATHOLYTICS to search ANTIMUSCARINIC AGENTS 1969-94
		MHTH	NLM (1995)
E12	0	UF	Agents, Antimuscarinic/CT
E13	0	UF	Antagonists, Muscarinic/CT
E14	0	UF	Antimuscarinic Agents/CT
E15	0	UF	MUSCARINIC ANTAG/CT
E16	20760	NT1	Atropine/CT
E17	1059	NT2	Atropine Derivatives/CT
E18	1323	NT3	Ipratropium/CT
E19	499	NT1	Benactyzine/CT
E20	553	NT1	Benztropine/CT
E21	325	NT1	Biperiden/CT
E22	291	NT1	Butylscopolammonium Bromide/CT
E23	221	NT1	Cyclopentolate/CT
E24	109	NT1	Dexetimide/CT
E25	127	NT1	Dicyclomine/CT
E26	116	NT1	Emepronium/CT
E27	478	NT1	Glycopyrrolate/CT
E28	334	NT1	Orphenadrine/CT
E29	111	NT1	Oxyphenonium/CT
E30	3192	NT1	Pirenzepine/CT
E31	153	NT1	Procyclidine/CT
E32	503	NT1	Propantheline/CT
E33	107	NT1	Propylbenzilylcholine Mustard/CT
E34	4551	NT1	Quinidine/CT
E35	1967	NT1	Quinuclidinyl Benzilate/CT

*muscarinic  
antagonists  
according to  
Medline*

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E36	4678	NT1	Scopolamine/CT
E37	1138	NT2	Scopolamine Derivatives/CT
E38	291	NT3	Butylscopolammonium Bromide/CT
E39	833	NT3	N-Methylscopolamine/CT
E40	642	NT1	Trihexyphenidyl/CT
E41	283	NT1	Tropicamide/CT
E42	9615	RT	Parasympatholytics/CT
*****	END***		

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TITLE: The pharmacological treatment of urinary incontinence.  
AUTHOR: Andersson K E; Appell R; Cardozo L D; Chapple C; Drutz H P;  
Finkbeiner A E; Haab F; Vela Navarrete R  
CORPORATE SOURCE: The Department of Clinical Pharmacology, Lund University  
Hospital, Lund, Sweden.. Karl-Erik.Andersson@klinfarm.lu.se  
SOURCE: BJU INTERNATIONAL, (1999 Dec) 84 (9) 923-47. Ref: 280  
Journal code: DCU; 100886721. ISSN: 1464-4096.  
PUB. COUNTRY: ENGLAND: United Kingdom  
Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW LITERATURE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200001  
ENTRY DATE: Entered STN: 20000204  
Last Updated on STN: 20000204  
Entered Medline: 20000127

L118 ANSWER 2 OF 73 MEDLINE DUPLICATE 4  
ACCESSION NUMBER: 94167741 MEDLINE  
DOCUMENT NUMBER: 94167741 PubMed ID: 7907192  
TITLE: Effects of intravesically administered anticholinergics,  
beta-adrenergic stimulant and alpha-adrenergic blocker on  
bladder function in unanesthetized rats.  
AUTHOR: Okimura O  
CORPORATE SOURCE: Department of Urology, Kyoto Prefectural University of  
Medicine.  
SOURCE: TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1993 Aug) 170 (4)  
251-60.  
Journal code: VTF; 0417355. ISSN: 0040-8727.  
PUB. COUNTRY: Japan  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199404  
ENTRY DATE: Entered STN: 19940412  
Last Updated on STN: 19950206  
Entered Medline: 19940405

AB Comparative analysis of the effects of intravesical instillation of drugs  
on urodynamic parameters (MVP, maximum intravesical pressure; RR, residual  
rate; BC, bladder capacity) was performed using an experimental model in  
unanesthetized rats. The drugs investigated in this study were atropine  
( $7.2 \times 10^{-4}$ - $7.2 \times 10^{-2}$  M), propantheline ( $7.2 \times 10^{-3}$ - $2.2 \times 10^{-2}$   
M), oxybutynin ( $2.5 \times 10^{-3}$ - $2.5 \times 10^{-2}$  M), isoproterenol ( $5 \times$   
 $10^{-2}$ - $10^{-1}$  M) and prazosin ( $5 \times 10^{-4}$  M). Of the anticholinergics,  
propantheline and oxybutynin showed a remarkable suppression of  
MVP accompanied with a consistent increase of RR and BC in a  
dose-dependent manner. Atropine showed, however, no suppression of MVP in  
spite of a significant change of RR and BC. Isoproterenol suppressed MVP  
with an increase of RR and BC in a dose-dependent manner at a relatively  
high concentration. Prazosin increased BC and RR at a relatively low  
concentration. This study revealed that these intravesical drugs have the  
ability to suppress spontaneous bladder contraction in unanesthetized rats  
and to change the micturition function in the urinary filling and storage  
phases. It is expected that intravesical instillation therapy for detrusor  
hyperreflexia will be improved in the future based upon the data obtained.

L118 ANSWER 3 OF 73 MEDLINE  
ACCESSION NUMBER: 2001145109 MEDLINE  
DOCUMENT NUMBER: 20567028 PubMed ID: 11114562  
TITLE: Advancements in pharmacologic management of the overactive  
bladder.  
AUTHOR: Dmochowski R R; Appell R A

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=> fil reg

FILE 'REGISTRY' ENTERED AT 10:27:52 ON 04 JUN 2003  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 3 JUN 2003 HIGHEST RN 524916-37-8  
DICTIONARY FILE UPDATES: 3 JUN 2003 HIGHEST RN 524916-37-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP  
PROPERTIES for more information. See STNote 27, Searching Properties  
in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> e tetrazosin/cn

E1	1	TETRAZOMINE DIHYDROCHLORIDE/CN
E2	1	TETRAZONE/CN
E3	0 -->	TETRAZOSIN/CN <i>assumed inventor meant terazosin</i>
E4	1	TETRAZOTIZED 3,3'-DICHLOROBENZIDINE/CN
E5	1	TETRAZOTIZED 4,4'-DIAMINO STILBENE/CN
E6	1	TETRAZOTIZED 4,4'-DIAMINO-2,2',5,5'-TETRAMETHYLTRIPHENYLMETH ANE/CN
E7	1	TETREHYMANOL/CN
E8	1	TETREN/CN
E9	1	TETRENE/CN
E10	1	TETRENOLIN/CN
E11	1	TETRETHYL/CN
E12	1	TETRETHYLENE GLYCOL DIMETHACRYLATE-N-VINYLCARBAZOLE COPOLYME R/CN

=> fil capl; d que 133

FILE 'CAPLUS' ENTERED AT 11:57:03 ON 04 JUN 2003

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FILE COVERS 1907 - 4 Jun 2003 VOL 138 ISS 23

FILE LAST UPDATED: 3 Jun 2003 (20030603/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L4	1	SEA FILE=REGISTRY ABB=ON	210538-44-6
L5	3	SEA FILE=REGISTRY ABB=ON	DOXAZOSIN?/CN
L6	3	SEA FILE=REGISTRY ABB=ON	TERAZOSIN?/CN
L7	1	SEA FILE=REGISTRY ABB=ON	ABANOQUIL/CN
L8	5	SEA FILE=REGISTRY ABB=ON	PRAZOSIN?/CN
L9	5	SEA FILE=REGISTRY ABB=ON	INDORAMIN?/CN
L10	2	SEA FILE=REGISTRY ABB=ON	DARIFENACIN?/CN
L11	2	SEA FILE=REGISTRY ABB=ON	TOLTERODINE?/CN
L12	3	SEA FILE=REGISTRY ABB=ON	OXYBUTYNIN?/CN
L13	2860	SEA FILE=CAPLUS ABB=ON	ADRENOCEPTOR ANTAGONISTS+OLD/CT(L)ALPHA
L14	1702	SEA FILE=CAPLUS ABB=ON	ALPHA(L) (ADRENOCEPTOR ANTAGONIST#)/OBI
L15	2879	SEA FILE=CAPLUS ABB=ON	(L4 OR L5 OR L6 OR L7 OR L8 OR L9)
L16	2566	SEA FILE=CAPLUS ABB=ON	(DOXAZOSIN# OR TETRAZOSIN# OR TERAZOSIN# OR ABANOQUIL# OR PRAZOSIN# OR INDORAMIN#)/OBI
L17	1465	SEA FILE=CAPLUS ABB=ON	MUSCARINIC ANTAGONISTS+OLD/CT
L18	1859	SEA FILE=CAPLUS ABB=ON	MUSCARINIC(2A)ANTAGONIST#/OBI
L19	472	SEA FILE=CAPLUS ABB=ON	(L10 OR L11 OR L12)
L20	479	SEA FILE=CAPLUS ABB=ON	(DARIFENACIN# OR TOLTERODIN# OR OXYBUTYNIN#)/OBI
L21	27544	SEA FILE=CAPLUS ABB=ON	DRUG INTERACTIONS+OLD/CT
L22	1888	SEA FILE=CAPLUS ABB=ON	DRUG DELIVERY SYSTEMS+OLD/CT(L)COMBIN?
L32	27544	SEA FILE=CAPLUS ABB=ON	DRUG INTERACTIONS+NT/CT OR L21
L33	5	SEA FILE=CAPLUS ABB=ON	(L13 OR L14 OR L15 OR L16) AND (L17 OR L18 OR L19 OR L20) AND (L22 OR L32)

=> fil medl; d que 159; d que 167; d que 176; d que 184; d que 185

FILE 'MEDLINE' ENTERED AT 11:57:04 ON 04 JUN 2003

FILE LAST UPDATED: 3 JUN 2003 (20030603/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L4 1 SEA FILE=REGISTRY ABB=ON 210538-44-6  
L5 3 SEA FILE=REGISTRY ABB=ON DOXAZOSIN?/CN  
L6 3 SEA FILE=REGISTRY ABB=ON TERAZOSIN?/CN  
L7 1 SEA FILE=REGISTRY ABB=ON ABANOQUIL/CN  
L8 5 SEA FILE=REGISTRY ABB=ON PRAZOSIN?/CN  
L9 5 SEA FILE=REGISTRY ABB=ON INDORAMIN?/CN  
L10 2 SEA FILE=REGISTRY ABB=ON DARIFENACIN?/CN  
L11 2 SEA FILE=REGISTRY ABB=ON TOLTERODINE?/CN  
L12 3 SEA FILE=REGISTRY ABB=ON OXYBUTYNIN?/CN  
L36 6827 SEA FILE=MEDLINE ABB=ON (L4 OR L5 OR L6 OR L7 OR L8 OR L9)  
L37 6643 SEA FILE=MEDLINE ABB=ON DOXAZOSIN/CT OR PRAZOSIN/CT  
L38 529 SEA FILE=MEDLINE ABB=ON TETRAZOSIN# OR TERAZOSIN# OR HYTRIN#  
OR A45975 OR A 45975 OR ABANOQUIL OR UK52046 OR UK 52046  
L39 283 SEA FILE=MEDLINE ABB=ON INDORAMIN# OR WY21901 OR WY 21901  
L40 475 SEA FILE=MEDLINE ABB=ON (L10 OR L11 OR L12)  
L41 652 SEA FILE=MEDLINE ABB=ON DARIFEN!CIN# OR TOLTERODIN# OR DETROL  
OR OXYBUTYNIN# OR CYSTRIN# OR OXYTROL#  
L59 4 SEA FILE=MEDLINE ABB=ON (L36 OR L37 OR L38 OR L39) AND (L40  
OR L41)

L53 10288 SEA FILE=MEDLINE ABB=ON ADRENERGIC ALPHA-ANTAGONISTS/CT  
L54 3097 SEA FILE=MEDLINE ABB=ON MUSCARINIC ANTAGONISTS/CT  
L63 9197 SEA FILE=MEDLINE ABB=ON L53(L) (AD OR PD OR PK OR TU)/CT  
L64 2414 SEA FILE=MEDLINE ABB=ON L54(L) (AD OR PD OR PK OR TU)/CT  
L66 105405 SEA FILE=MEDLINE ABB=ON DRUG COMBINATIONS+NT/CT OR DRUG  
THERAPY, COMBINATION/CT  
L67 3 SEA FILE=MEDLINE ABB=ON L63 AND L64 AND L66

L35 885 SEA FILE=MEDLINE ABB=ON RECEPTORS, ADRENERGIC, ALPHA+NT/CT(L)A  
I/CT  
L46 37197 SEA FILE=MEDLINE ABB=ON ADRENERGIC ALPHA-ANTAGONISTS+NT/CT  
L47 40225 SEA FILE=MEDLINE ABB=ON MUSCARINIC ANTAGONISTS+NT/CT  
L66 105405 SEA FILE=MEDLINE ABB=ON DRUG COMBINATIONS+NT/CT OR DRUG  
THERAPY, COMBINATION/CT  
L74 682 SEA FILE=MEDLINE ABB=ON L66/MAJ  
L76 2 SEA FILE=MEDLINE ABB=ON (L35 OR L46) AND L47 AND L74

L35 885 SEA FILE=MEDLINE ABB=ON RECEPTORS, ADRENERGIC, ALPHA+NT/CT(L)A  
I/CT  
L46 37197 SEA FILE=MEDLINE ABB=ON ADRENERGIC ALPHA-ANTAGONISTS+NT/CT  
L47 40225 SEA FILE=MEDLINE ABB=ON MUSCARINIC ANTAGONISTS+NT/CT  
L66 105405 SEA FILE=MEDLINE ABB=ON DRUG COMBINATIONS+NT/CT OR DRUG  
THERAPY, COMBINATION/CT  
L69 32753 SEA FILE=MEDLINE ABB=ON L46(L) (AD OR PD OR PK OR TU)/CT  
L70 32995 SEA FILE=MEDLINE ABB=ON L47(L) (AD OR PD OR PK OR TU)/CT  
L79 4551 SEA FILE=MEDLINE ABB=ON QUINIDINE/CT  
L80 32861 SEA FILE=MEDLINE ABB=ON (L35 OR L46) NOT L79  
L81 35674 SEA FILE=MEDLINE ABB=ON L47 NOT L79  
L82 32 SEA FILE=MEDLINE ABB=ON L80 AND L81 AND L66

*subheading  
AI = antagonists  
& inhibitors*

*Medline considers this an  $\alpha$  adrenergic  
receptor antagonist & a  
muscarinic antagonist,  
so I had to remove  
it from the answer  
set*

L84            5 SEA FILE=MEDLINE ABB=ON L69/MAJ AND L70/MAJ AND L82

L35           885 SEA FILE=MEDLINE ABB=ON RECEPTORS, ADRENERGIC, ALPHA+NT/CT(L)A  
I/CT

L46           37197 SEA FILE=MEDLINE ABB=ON ADRENERGIC ALPHA-ANTAGONISTS+NT/CT

L47           40225 SEA FILE=MEDLINE ABB=ON MUSCARINIC ANTAGONISTS+NT/CT

L66           105405 SEA FILE=MEDLINE ABB=ON DRUG COMBINATIONS+NT/CT OR DRUG  
THERAPY, COMBINATION/CT

L79           4551 SEA FILE=MEDLINE ABB=ON QUINIDINE/CT

L80           32861 SEA FILE=MEDLINE ABB=ON (L35 OR L46) NOT L79

L81           35674 SEA FILE=MEDLINE ABB=ON L47 NOT L79

L82           32 SEA FILE=MEDLINE ABB=ON L80 AND L81 AND L66

L85           1 SEA FILE=MEDLINE ABB=ON GENERAL REVIEW/DT AND L82

=> s 159 or 167 or 176 or 184 or 185

L139           14 L59 OR L67 OR L76 OR L84 OR L85

=> fil embase; d que 1107;d que 1113

FILE 'EMBASE' ENTERED AT 11:57:06 ON 04 JUN 2003  
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FILE COVERS 1974 TO 29 May 2003 (20030529/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

L86           5910 SEA FILE=EMBASE ABB=ON ALPHA ADRENERGIC RECEPTOR BLOCKING  
AGENT/CT

L88           2306 SEA FILE=EMBASE ABB=ON DOXAZOSIN/CT OR DOXAZOSIN DERIVATIVE/CT  
OR DOXAZOSIN MESYLATE/CT

L89           1452 SEA FILE=EMBASE ABB=ON TERAZOSIN/CT

L90           37 SEA FILE=EMBASE ABB=ON ABANOQUIL/CT

L91           16803 SEA FILE=EMBASE ABB=ON PRAZOSIN/CT OR PRAZOSIN DERIVATIVE/CT

L92           704 SEA FILE=EMBASE ABB=ON INDORAMIN/CT OR INDORAMIN DERIVATIVE/CT

L93           2282 SEA FILE=EMBASE ABB=ON MUSCARINIC RECEPTOR BLOCKING AGENT/CT

L95           92 SEA FILE=EMBASE ABB=ON DARIFENACIN/CT

L96           410 SEA FILE=EMBASE ABB=ON TOLTERODINE/CT OR TOLTERODINE TARTRATE/  
CT

L97           1627 SEA FILE=EMBASE ABB=ON OXYBUTYNIN/CT

L105          1212 SEA FILE=EMBASE ABB=ON (L86 OR (L88 OR L89 OR L90 OR L91 OR  
L92)) (L)CB/CT

L106          191 SEA FILE=EMBASE ABB=ON (L93 OR (L95 OR L96 OR L97)) (L)CB/CT

L107          8 SEA FILE=EMBASE ABB=ON L105 AND L106

*subheading  
CB = drug  
combination*

L86           5910 SEA FILE=EMBASE ABB=ON ALPHA ADRENERGIC RECEPTOR BLOCKING  
AGENT/CT

L88           2306 SEA FILE=EMBASE ABB=ON DOXAZOSIN/CT OR DOXAZOSIN DERIVATIVE/CT  
OR DOXAZOSIN MESYLATE/CT

L89           1452 SEA FILE=EMBASE ABB=ON TERAZOSIN/CT

L90           37 SEA FILE=EMBASE ABB=ON ABANOQUIL/CT

L91           16803 SEA FILE=EMBASE ABB=ON PRAZOSIN/CT OR PRAZOSIN DERIVATIVE/CT

L92           704 SEA FILE=EMBASE ABB=ON INDORAMIN/CT OR INDORAMIN DERIVATIVE/CT

L93 2282 SEA FILE=EMBASE ABB=ON MUSCARINIC RECEPTOR BLOCKING AGENT/CT  
L95 92 SEA FILE=EMBASE ABB=ON DARIFENACIN/CT  
L96 410 SEA FILE=EMBASE ABB=ON TOLTERODINE/CT OR TOLTERODINE TARTRATE/  
CT  
L97 1627 SEA FILE=EMBASE ABB=ON OXYBUTYNIN/CT  
L108 251 SEA FILE=EMBASE ABB=ON (L93 OR (L95 OR L96 OR L97)) (L) IT/CT  
L109 860 SEA FILE=EMBASE ABB=ON (L86 OR (L88 OR L89 OR L90 OR L91 OR  
L92)) (L) IT/CT  
L112 1364 SEA FILE=EMBASE ABB=ON BLADDER CONTRACTION/CT  
L113 1 SEA FILE=EMBASE ABB=ON L108 AND L109 AND L112

=> s 1107 or 1113

L140 9 L107 OR L113

=> fil wpids; d que 1137

FILE 'WPIDS' ENTERED AT 11:57:07 ON 04 JUN 2003  
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FILE LAST UPDATED: 3 JUN 2003 <20030603/UP>  
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L116 508 SEA FILE=WPIDS ABB=ON (ADRENOCEPTOR OR ADRENERGIC) (2A) ALPHA (2A  
) (ANTAGONIST# OR BLOCK?)  
L117 112 SEA FILE=WPIDS ABB=ON DOXAZOSIN# OR CARDURA# OR UK33274 OR UK  
33274  
L118 79 SEA FILE=WPIDS ABB=ON TETRAZOSIN# OR TERAZOSIN# OR HYTRIN# OR  
A45975 OR A 45975  
L119 4 SEA FILE=WPIDS ABB=ON ABANOQUIL# OR UK52046 OR UK 52046  
L120 200 SEA FILE=WPIDS ABB=ON PRAZOSIN# OR FURAZOSIN# OR PRATSIOL#  
L121 31 SEA FILE=WPIDS ABB=ON INDORAMIN# OR WY21901 OR WY 21901  
L122 183 SEA FILE=WPIDS ABB=ON MUSCARINIC (2A) (ANTAGONIST# OR BLOCK?)  
L123 124 SEA FILE=WPIDS ABB=ON DARIFEN!CIN# OR TOLTERODIN# OR DETROL  
OR OXYBUTYNIN# OR CYSTRIN# OR OXYTROL#  
L130 781663 SEA FILE=WPIDS ABB=ON COMBIN? OR SIMULTANEOUS? OR SEQUENTIAL?  
L136 373681 SEA FILE=WPIDS ABB=ON MIXTUR?  
L137 5 SEA FILE=WPIDS ABB=ON (L116 OR L117 OR L118 OR L119 OR L120  
OR L121) AND (L122 OR L123) AND (L130 OR L136)

=> dup rem 133,1139,1140,1137

FILE 'CAPLUS' ENTERED AT 11:57:30 ON 04 JUN 2003

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COPYRIGHT (C) 2003 THOMSON DERWENT  
PROCESSING COMPLETED FOR L33  
PROCESSING COMPLETED FOR L139  
PROCESSING COMPLETED FOR L140  
PROCESSING COMPLETED FOR L137.  
L141 31 DUP REM L33 L139 L140 L137 (2 DUPLICATES REMOVED)  
ANSWERS '1-5' FROM FILE CAPLUS  
ANSWERS '6-19' FROM FILE MEDLINE  
ANSWERS '20-28' FROM FILE EMBASE  
ANSWERS '29-31' FROM FILE WPIDS

=> d ibib ab hitrn 1-5; d iall 6-31

L141 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1  
ACCESSION NUMBER: 2001:594376 CAPLUS  
DOCUMENT NUMBER: 135:185453  
TITLE: Pharmaceutical combinations for treating lower urinary  
tract disfunctions  
INVENTOR(S): Wyllie, Michael Grant  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: Eur. Pat. Appl., 13 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1123705	A1	20010816	EP 2001-301085	20010207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2334460	AA	20010809	CA 2001-2334460	20010207
US 2001044438	A1	20011122	US 2001-778290	20010207
NZ 509807	A	20020927	NZ 2001-509807	20010208
PRIORITY APPLN. INFO.:		US 2000-181310P P 20000209		
AB	Pharmaceutical combinations suitable for treating the lower urinary tract symptoms assocd. with benign prostatic hyperplasia in men contain an .alpha.-adrenoceptor antagonist and a muscarinic antagonist. The combinations of the invention are particularly suitable for treating moderate or severe lower urinary tract symptoms. Thus, tablet contained doxazosin mesylate 4.05, microcryst. cellulose 125.28, lactose 66.67, sodium starch glycolate 2.00, and Mg stearate 2.00% by wt.			
IT	5633-20-5, Oxybutynin 19216-56-9, Prazosin 26844-12-2, Indoramine 63590-64-7, Terazosin 74191-85-8, Doxazosin 77883-43-3, Doxazosin mesylate 90402-40-7, Abanoquil 124937-51-5, Tolterodine 133099-04-4, Darifenacin 133099-07-7, Darifenacin hydrobromide 210538-44-6 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceutical combinations for treating lower urinary tract			

disfunctions)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2  
ACCESSION NUMBER: 2000:725447 CAPLUS  
DOCUMENT NUMBER: 133:301178  
TITLE: Use of CYP2D6 inhibitors in combination therapies  
INVENTOR(S): Obach, Ronald Scott  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 18 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059486	A2	20001012	WO 2000-IB304	20000320
WO 2000059486	C1	20020725		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000009564	A	20020108	BR 2000-9564	20000320
EP 1242058	A1	20020925	EP 2000-909570	20000320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
EE 200100524	A	20021216	EE 2001-524	20000320
NO 2001004858	A	20011205	NO 2001-4858	20011005
BG 106075	A	20020628	BG 2001-106075	20011101
PRIORITY APPLN. INFO.: US 1999-128136P P 19990407				
WO 2000-IB304 W 20000320				
AB This invention relates to the use of a CYP2D6 inhibitor in combination with a drug having CYP2D6-catalyzed metab., wherein the drug and the CYP2D6 inhibitor are not the same compd.; and pharmaceutical compns. for said use.				
IT 5633-20-5, Oxybutynin 26844-12-2, Indoramin 124937-51-5, Tolterodine				
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (use of CYP2D6 inhibitors in combination therapies)				

L141 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2003:147944 CAPLUS  
DOCUMENT NUMBER: 138:193282  
TITLE: Use of .alpha.-adrenoceptor antagonist in combination with muscarinic antagonist for medicament  
INVENTOR(S): Wayley, Michael Grant  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: Jpn. Kokai Tokkyo Koho, 36 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2003055261	A2	20030226	JP 2001-240717	20010808
PRIORITY APPLN. INFO.:			JP 2001-240717	20010808
AB The invention relates to pharmaceutical combinations suitable for treating the lower urinary tract symptoms (LUTS) assocd. with benign prostatic hyperplasia (BPH) in men, which combinations contain an .alpha.-adrenoceptor antagonist and a muscarinic antagonist. The combinations of the invention are particularly suitable for treating moderate or severe LUTS. A combination immediate-release darifenacin/doxazosin tablet contg. doxazosin mesylate 4.05, darifenacin hydrobromide 2.976, microcryst. cellulose 125.28, lactose 63.694, sodium starch glycollate 2, magnesium stearate 2 mg was prepd.				
IT 5633-20-5, Oxybutynin 19216-56-9, Prazosin 26844-12-2, Indoramin 74191-85-8, Doxazosin 77883-43-3, Doxazosin mesylate 90402-40-7, Abanoquil 124937-51-5, Tolterodine 133099-04-4, Darifenacin 133099-07-7, Darifenacin hydrobromide 210538-44-6				
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (use of .alpha.-adrenoceptor antagonist in combination with muscarinic antagonist for treatment of benign prostatic hyperplasia)				

L141 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:153396 CAPLUS

DOCUMENT NUMBER: 138:180766

TITLE: Use of BIBN4096BS in combination with other antimigraine medications for the treatment of headache, migraine or cluster headache

INVENTOR(S): Doods, Henri; Hurnaus, Rudolf; Eberlein, Wolfgang

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany

SOURCE: Ger. Offen., 14 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10139410	A1	20030227	DE 2001-10139410	20010817
WO 2003015787	A1	20030227	WO 2002-EP8993	20020810
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: DE 2001-10139410 A 20010817

AB The invention provides a method for the treatment or prevention of headache, migraine, or cluster headache, which involves the common administration of a therapeutically effective amt. of 1-[N2-[3,5-dibromo-N-[[4-(3,4-dihydro-2(1H)-oxoquinazoline-3-yl)-1-piperidinyl]-carbonyl]-D-tyrosyl]-L-lysyl]-4-(4-pyridinyl)-piperazine

[BIBN4096BS], or a physiol. acceptable salt thereof, and a therapeutically effective amt. of a second active antimigraine medication, in particular sumatriptan, zolmitriptan, or dihydroergotamine, or a physiol. acceptable salt thereof. Pharmaceutical compns. and prodn. thereof are also provided.

L141 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:157574 CAPLUS

DOCUMENT NUMBER: 136:210605

TITLE: Method of treating or preventing urinary incontinence using prostanoid EP1 receptor antagonists

INVENTOR(S): Broten, Theodore P.; Nantel, Francois J.; Metters, Kathleen M.; Turner, Mervyn

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Merck Frosst Canada & Co.

SOURCE: PCT Int. Appl., 127 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002015902	A1	20020228	WO 2001-US25982	20010820
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2001086557	A5	20020304	AU 2001-86557	20010820
US 2002137746	A1	20020926	US 2001-935614	20010823
PRIORITY APPLN. INFO.:			US 2000-227183P P	20000823
			WO 2001-US25982 W	20010820

OTHER SOURCE(S): MARPAT 136:210605

AB This invention encompasses a method of treating or preventing urinary incontinence in a mammalian patient comprising administering to the patient a compd. of formula I (X = C or N; x and z are independently 0-2 such that y + z = 2; Ra = heteroaryl such as furyl, diazinyl, triazinyl, tetrazinyl, imidazolyl, isoxazolyl, isothiazolyl, etc.; R1, R2, R3, R4 and R5 are independently = H, halogen, C1-6alkyl, C1-6alkoxy, C1-6alkylthio, etc.; R6 = H, OH, C1-6alkyl, C1-6alkoxy, etc.) or a pharmaceutically acceptable salt, hydrate or ester thereof. The invention also encompasses certain pharmaceutical compns. and methods for treatment of prostaglandin mediated diseases comprising the use of compds. of formula I.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L141 ANSWER 6 OF 31 MEDLINE

ACCESSION NUMBER: 2002164226 MEDLINE

DOCUMENT NUMBER: 21893170 PubMed ID: 11896476

TITLE: Intracavernous injections for erectile dysfunction in patients with cardiovascular diseases and failure or contraindications for sildenafil citrate.

AUTHOR: Israilov S; Niv E; Livne P M; Shmueli J; Engelstein D; Segenreich E; Baniel J

CORPORATE SOURCE: Institute of Urology, Rabin Medical Center, Beilinson

SOURCE: Campus, Petah Tiqva 49110, Israel.  
INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH, (2002 Feb) 14  
(1) 38-43.  
Journal code: 9007383. ISSN: 0955-9930.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200206  
ENTRY DATE: Entered STN: 20020317  
Last Updated on STN: 20020620  
Entered Medline: 20020619

**ABSTRACT:**

The aim of this study was to evaluate the effectiveness of a progressive program for the treatment of erectile dysfunction in patients with cardiovascular disease in whom sildenafil citrate (Viagra) was not an option. The study population included 106 patients selected from 267 with cardiovascular disease. The intracavernous injection program consisted of three protocols of increasingly complex combinations of vasoactive drugs, papaverine, phentolamine, prostaglandin E1 and atropine sulfate. Patients who failed the first protocol were switched to the second, and those who failed the second were switched to the third. A positive response was defined as an erection sufficient for vaginal penetration. A positive response was achieved on protocol I in 61 of the 106 patients (57.5%); protocol II in 32 of the remaining 45 patients (71.1%); and protocol III in seven of the remaining 13 patients (53.8%); the total success rate was 94.3%. These 100 patients were included in the 1-year follow-up, and 90 reported successful coitus at the end of that period: 79 patients (87.8%) with intracavernous injection and 11 (12.2%) without injection. The remaining 10 patients (10%) dropped out of the program, seven (7.0%) for health or marital reasons and three (3.0%) because of treatment failure. We conclude that a progressive program of intracavernous injections of vasoactive drugs may be a good alternative for the treatment of erectile dysfunction in patients with cardiovascular disease.

CONTROLLED TERM: Check Tags: Human; Male

**Adrenergic alpha-Antagonists: AD, administration & dosage**

Adrenergic alpha-Antagonists: AE, adverse effects

**Adrenergic alpha-Antagonists: TU, therapeutic use**

Adult

Aged

Aged, 80 and over

Alprostadil: AD, administration & dosage

Alprostadil: AE, adverse effects

Alprostadil: TU, therapeutic use

Atropine: AD, administration & dosage

Atropine: AE, adverse effects

Atropine: TU, therapeutic use

\*Cardiovascular Diseases: CO, complications

Coitus

**Drug Combinations**

Follow-Up Studies

\*Impotence: CO, complications

\*Impotence: DT, drug therapy

Injections

Middle Age

**Muscarinic Antagonists: AD, administration & dosage**

Muscarinic Antagonists: AE, adverse effects

**Muscarinic Antagonists: TU, therapeutic use**

Papaverine: AD, administration & dosage

Papaverine: AE, adverse effects

Papaverine: TU, therapeutic use

Penis

Phentolamine: AD, administration & dosage  
Phentolamine: AE, adverse effects  
Phentolamine: TU, therapeutic use  
Piperazines: CT, contraindications  
Piperazines: TU, therapeutic use  
Retreatment  
Treatment Failure  
\*Vasodilator Agents: AD, administration & dosage  
Vasodilator Agents: AE, adverse effects  
Vasodilator Agents: CT, contraindications  
Vasodilator Agents: TU, therapeutic use

CAS REGISTRY NO.: 139755-83-2 (sildenafil); 50-60-2 (Phentolamine); 51-55-8 (Atropine); 58-74-2 (Papaverine); 745-65-3 (Alprostadil)  
CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Drug Combinations); 0 (Muscarinic Antagonists); 0 (Piperazines); 0 (Vasodilator Agents)

L141 ANSWER 7 OF 31 MEDLINE  
ACCESSION NUMBER: 2002045730 MEDLINE  
DOCUMENT NUMBER: 21629702 PubMed ID: 11755385  
TITLE: Influence of pump compliance (peristaltic vs. infusion) on urodynamic measurement during cystometry in conscious rats.  
AUTHOR: Velasco C; Guarneri L; Leonardi A; Testa R  
CORPORATE SOURCE: Pharmaceutical R & D Division-Recordati S.p.A., Mia M. Civitali I-20148, Milano, Italy.  
SOURCE: JOURNAL OF PHARMACOLOGICAL AND TOXICOLOGICAL METHODS, (2001 May-Jun) 45 (3) 215-21.  
Journal code: 9206091. ISSN: 1056-8719.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200202  
ENTRY DATE: Entered STN: 20020124  
Last Updated on STN: 20020301  
Entered Medline: 20020228

## ABSTRACT:

Cystometry, employing natural or pump-induced bladder filling, is the most widely used method for studying bladder reflexes and micturition in conscious rats. However, discrepancies in basal values of urodynamic parameters are often reported, especially for micturition pressure. The aim of this study was to establish whether the type of pump used (peristaltic or infusion) might yield different urodynamic parameters. Differences between natural filling (evaluated in water-loaded animals and considered "physiological micturition") and pump-evoked cystometrograms, as well as the compliance of these systems, and the effects of pharmacologically diverse drugs (prazosin, \*\*\*oxybutynin\*\*\*, and naproxen) acting on the bladder voiding were evaluated. Micturition pressure recorded from pump-evoked cystometrograms showed differences from natural micturition that were related to the total compliance of the system (pump + tube) and not only to the nature of the pump used. Drug-induced changes of micturition pressure during natural micturition resembled those recorded during bladder infusion with a peristaltic pump more than those with an infusion pump. Other basal values and drug-induced changes of bladder capacity were the same during natural and pump-evoked micturition. The present findings indicate that cystometrographic parameters obtained during pump-evoked micturition with a system at high compliance (peristaltic pump) are equivalent to those observed during physiological micturition.

CONTROLLED TERM: Check Tags: Animal; Comparative Study; Male  
Bladder: DE, drug effects  
\*Bladder: PH, physiology  
Consciousness  
\*Infusion Pumps, Implantable  
Mandelic Acids: PD, pharmacology

Naproxen: PD, pharmacology  
Prazosin: PD, pharmacology  
Rats  
Rats, Sprague-Dawley  
Reproducibility of Results  
Urinary Catheterization: IS, instrumentation  
Urinary Catheterization: MT, methods  
Urination: DE, drug effects  
Urination: PH, physiology  
Urodynamics: DE, drug effects  
\*Urodynamics: PH, physiology

CAS REGISTRY NO.: 19216-56-9 (Prazosin); 22204-53-1 (Naproxen);  
5633-20-5 (oxybutynin)  
CHEMICAL NAME: 0 (Mandelic Acids)

L141 ANSWER 8 OF 31 MEDLINE

ACCESSION NUMBER: 1999180092 MEDLINE  
DOCUMENT NUMBER: 99180092 PubMed ID: 10082055  
TITLE: The clinical efficacy of paremyd with and without  
dapiprazole in subjects with light and dark brown irides.  
AUTHOR: Anicho U M; Cooper J; Feldman J; Jaanus S D; Dignam K  
CORPORATE SOURCE: Schnurmacher Institute for Vision Research, State  
University of New York, State College of Optometry, New  
York 10010-3677, USA.  
SOURCE: OPTOMETRY AND VISION SCIENCE, (1999 Feb) 76 (2) 94-101.  
Journal code: 8904931. ISSN: 1040-5488.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(RANDOMIZED CONTROLLED TRIAL)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199905  
ENTRY DATE: Entered STN: 19990517  
Last Updated on STN: 19990517  
Entered Medline: 19990504

ABSTRACT:

BACKGROUND: Paremyd, a mydriatic formulation of 0.25% tropicamide and 1.0% hydroxyamphetamine hydrobromide provides adequate dilation for binocular indirect ophthalmoscopy in young Caucasians. We studied the clinical effectiveness of Paremyd in dilating heavily pigmented eyes by comparing its mydriatic efficacy in Blacks, Asians and Caucasians with light and dark brown irides. We also evaluated the efficacy of one drop of dapiprazole (Rev-Eyes) in reversing Paremyd-induced mydriasis in our subject sample. METHODS: In a masked, randomized, controlled experimental design, several visual functions which included pupillary dilation, near visual acuity, amplitude of accommodation, ocular hyperemia, and discomfort glare were measured at 30-min intervals, for a total of 300 min, in subjects dilated with a single drop of Paremyd in each eye. Ease of binocular indirect ophthalmoscopy was also assessed. A 3-way analysis of variance was used to assess changes in these measures as function of irides color/pigmentation (designated as light or dark brown iris color), presence or absence of dapiprazole, and test time interval. RESULTS: We found that subjects in our light brown irides group (mainly Caucasians) dilated faster than subjects in our dark brown irides group (mainly Blacks). Dapiprazole increased the speed of recovery from pupillary dilation for all subjects, but more so for those with light rather than dark brown irides. Similarly, subjects with light rather than dark brown irides recovered accommodative function more quickly. Although neither the use of dapiprazole nor the degree of iris color/pigmentation was significantly related to visual acuity or glare discomfort, there was a clear trend that these visual measures were affected to a greater degree in subjects with dark brown (primarily Blacks) rather than light brown irides. Overall, Paremyd provided adequate dilation for binocular indirect ophthalmoscopy in all subjects irrespective of

iris color/pigmentation. CONCLUSIONS: Our data indicate that a single drop of Paremyd provides adequate mydriasis, without significant side effects, for routine fundus examination of all subjects, independent of iris color/pigmentation. Furthermore, a single drop of dapiprazole was effective in speeding the return of pupillary dilation in most subjects, but had no significant effect on accommodation, near visual acuity or glare discomfort. Side effects such as stinging upon instillation, conjunctival hyperemia, and a few instances of ptosis, with possible additional cost to patients, appear to lessen its overall clinical benefit.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't  
Accommodation, Ocular: DE, drug effects  
Adolescent

Adrenergic alpha-Antagonists: AD, administration & dosage

\*Adrenergic alpha-Antagonists: TU, therapeutic use  
Adult

Drug Therapy, Combination

\*Eye Color

Glare

Iris: DE, drug effects

Iris: PH, physiology

Mydriatics: AD, administration & dosage

\*Mydriatics: TU, therapeutic use

Ophthalmic Solutions: AD, administration & dosage

Ophthalmic Solutions: TU, therapeutic use

Ophthalmoscopy

\*Pupil: DE, drug effects

Triazoles: AD, administration & dosage

\*Triazoles: TU, therapeutic use

Tropicamide: AD, administration & dosage

\*Tropicamide: TU, therapeutic use

Visual Acuity: DE, drug effects

p-Hydroxyamphetamine: AD, administration & dosage

\*p-Hydroxyamphetamine: TU, therapeutic use

CAS REGISTRY NO.: 103-86-6 (p-Hydroxyamphetamine); 1508-75-4 (Tropicamide);  
72822-12-9 (dapiprazole)

CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Mydriatics); 0  
(Ophthalmic Solutions); 0 (Triazoles)

L141 ANSWER 9 OF 31

MEDLINE

ACCESSION NUMBER: 1998321928 MEDLINE

DOCUMENT NUMBER: 98321928 PubMed ID: 9660491

TITLE: Synergistic receptor-activated calcium increases in single nonpigmented epithelial cells.

AUTHOR: Cilluffo M C; Xia S L; Farahbakhsh N A; Fain G L

CORPORATE SOURCE: Department of Physiological Science, University of California, Los Angeles 90095-1527, USA.

CONTRACT NUMBER: EY06969 (NEI)

EY07568 (NEI)

SOURCE: INVESTIGATIVE OPHTHALMOLOGY AND VISUAL SCIENCE, (1998 Jul)  
39 (8) 1429-35.

Journal code: 7703701. ISSN: 0146-0404.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199807

ENTRY DATE: Entered STN: 19980723

Last Updated on STN: 19980723

Entered Medline: 19980714

ABSTRACT:

PURPOSE: To determine whether single nonpigmented ciliary body cells contain

the signaling mechanism to produce synergistic drug-activated increases in  $Ca^{2+}$ , or whether these responses are produced cooperatively by interaction among groups of cells. **METHODS:** Suspensions of single nonpigmented cells were plated onto soft collagen gels. Fura-2 fluorescence ratio imaging was used to examine receptor-evoked changes in intracellular  $Ca^{2+}$  concentration. **RESULTS:** Nonpigmented cells plated on soft collagen gels retained a rounded shape with membrane evaginations visible on their surface. Application of acetylcholine (10  $\mu M$ ) or epinephrine (1  $\mu M$ ) each produced small increases in intracellular  $Ca^{2+}$ , but in combination they produced a  $Ca^{2+}$  increase of more than 10-fold. This synergistic  $Ca^{2+}$  increase was a result of activation of muscarinic and  $\alpha_2$ -adrenergic receptors because a specific  $\alpha_2$ -adrenergic agonist could substitute for epinephrine in producing the response. The response could be blocked by a specific  $\alpha_2$ -antagonist and a muscarinic antagonist. An  $\alpha_1$ -agonist could not substitute for epinephrine in producing a synergistic increase nor could the synergism be blocked by  $\alpha_1$ - or  $\beta$ -antagonists. The  $Ca^{2+}$  increase was largely produced by release from internal stores, because the peak amplitude of the response was nearly the same in the external solution containing a low  $Ca^{2+}$  concentration; however, the influx of  $Ca^{2+}$  into the cell was responsible for maintenance of a steady component of the  $Ca^{2+}$  increase during maintained drug stimulation and for refilling the internal stores. **CONCLUSIONS:** Single nonpigmented cells can produce synergistic increases in  $Ca^{2+}$  on multiple receptor activation, indicating that the mechanism of synergism does not require the interaction of multiple cells. The  $Ca^{2+}$  increase is a result of release from internal stores and  $Ca^{2+}$  entry through an as yet undefined conductance or transport system in the plasma membrane.

**CONTROLLED TERM:** Check Tags: Animal; Support, U.S. Gov't, P.H.S.

Acetylcholine: PD, pharmacology

**Adrenergic alpha-Antagonists: PD, pharmacology**

\*Calcium: ME, metabolism

Cells, Cultured

Ciliary Body: CY, cytology

Ciliary Body: DE, drug effects

\*Ciliary Body: ME, metabolism

Collagen

**Drug Combinations**

Drug Synergism

Epinephrine: PD, pharmacology

Epithelial Cells: CY, cytology

Epithelial Cells: DE, drug effects

\*Epithelial Cells: ME, metabolism

Fluorescent Dyes: ME, metabolism

Fura-2: ME, metabolism

Gels

**Muscarinic Antagonists: PD, pharmacology**

Rabbits

\*Receptors, Adrenergic,  $\alpha_2$ : ME, metabolism

\*Receptors, Muscarinic: ME, metabolism

**CAS REGISTRY NO.:** 51-43-4 (Epinephrine); 51-84-3 (Acetylcholine); 7440-70-2

(Calcium); 9007-34-5 (Collagen); 96314-98-6 (Fura-2)

**CHEMICAL NAME:** 0 (Adrenergic alpha-Antagonists); 0 (Drug Combinations); 0 (Fluorescent Dyes); 0 (Gels); 0 (Muscarinic Antagonists); 0 (Receptors, Adrenergic,  $\alpha_2$ ); 0 (Receptors, Muscarinic)

L141 ANSWER 10 OF 31 MEDLINE

ACCESSION NUMBER: 1998114435 MEDLINE

DOCUMENT NUMBER: 98114435 PubMed ID: 9453690

**TITLE:** Prospective study comparing hyoscyamine, doxazosin, and combination therapy for the treatment of urgency and frequency in women.

**AUTHOR:** Serels S; Stein M

**CORPORATE SOURCE:** Department of Urology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, New York, USA.

SOURCE: NEUROUROLOGY AND URODYNAMICS, (1998) 17 (1) 31-6.  
Journal code: 8303326. ISSN: 0733-2467.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (CLINICAL TRIAL)  
(CONTROLLED CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199803  
ENTRY DATE: Entered STN: 19980326  
Last Updated on STN: 19980326  
Entered Medline: 19980318

## ABSTRACT:

Anticholinergics are commonly used for the treatment of frequency, urgency, and urge incontinence in women. Alpha-blockers have been shown to have a modulating effect on bladder smooth muscle but are not commonly used clinically for this indication. To evaluate the clinical effectiveness of each treatment as well as the combination therapy, we performed an open prospective study comparing these agents. Between September 1994 and October 1995, 34 women aged 28-91 (mean age, 62) received either 0.375 mg of sustained-release hyoscyamine twice a day or 2 mg doxazosin QHS prior to being crossed over to the other drug and/or the combination. Symptoms were assessed using an expanded American Urological Association (AUA) symptoms score, which included questions regarding incontinence at completion of each therapeutic phase. Evaluation included 6-channel urodynamics. All three therapies were noted to be effective in reducing AUA symptom scores. By urodynamic evaluation, a greater percentage of patients with increased voiding pressures or decreased compliance responded to doxazosin than hyoscyamine. Side effects were noted to be less prevalent with doxazosin than with the other therapies. There appears to be a significant role for alpha-blockers in the treatment of voiding symptoms in women.

CONTROLLED TERM: Check Tags: Comparative Study; Female; Human  
Adrenergic alpha-Antagonists: AE, adverse effects  
\*Adrenergic alpha-Antagonists: TU, therapeutic use  
Adult  
Aged  
Aged, 80 and over  
Atropine: AD, administration & dosage  
\*Atropine: TU, therapeutic use  
Bladder: DE, drug effects  
Bladder: PP, physiopathology  
Cross-Over Studies  
Delayed-Action Preparations  
Doxazosin: AE, adverse effects  
\*Doxazosin: TU, therapeutic use  
Drug Therapy, Combination  
Middle Age  
Muscarinic Antagonists: AD, administration & dosage  
dosage  
\*Muscarinic Antagonists: TU, therapeutic use  
Prospective Studies  
Safety  
Severity of Illness Index  
Treatment Outcome  
\*Urinary Incontinence: DT, drug therapy  
Urinary Incontinence: PP, physiopathology  
Urodynamics: DE, drug effects  
CAS REGISTRY NO.: 51-55-8 (Atropine); 74191-85-8 (Doxazosin)  
CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Delayed-Action Preparations); 0 (Muscarinic Antagonists)

L141 ANSWER 11 OF 31 MEDLINE  
ACCESSION NUMBER: 95299493 MEDLINE  
DOCUMENT NUMBER: 95299493 PubMed ID: 7780441

TITLE: Autonomic dysreflexia in a rat model spinal cord injury and the effect of pharmacologic agents.  
AUTHOR: Rivas D A; Chancellor M B; Huang B; Salzman S K  
CORPORATE SOURCE: Department of Urology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA 19107, USA.  
SOURCE: NEUROUROLOGY AND URODYNAMICS, (1995) 14 (2) 141-52.  
Journal code: 8303326. ISSN: 0733-2467.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199507  
ENTRY DATE: Entered STN: 19950726  
Last Updated on STN: 19950726  
Entered Medline: 19950720

## ABSTRACT:

The object of this study was to develop a spinal cord injury (SCI) rat model for autonomic dysreflexia (AD), assessing the effect of alpha-adrenergic and calcium channel blockade and to determine the relationship of detrusor-external sphincter dyssynergia (DESD) to the development of AD. A laminectomy was performed in male rats at the T4 or T10 level and a controlled 50 g cm blunt SCI was induced using an impounder. Four weeks after injury, changes in arterial blood pressure and heart rate were monitored while simultaneous cystometry (CMG) and pelvic floor electromyography (EMG) were performed in vivo in sham (control) and spinal cord injured rats. The effects of \*\*\*terazosin\*\*\* (0.1 mg/kg), diltiazem (0.5 mg/kg), and oxybutynin chloride (0.1 mg/kg) on hemodynamic changes were assessed independently. Both T4 and T10 SCI rat displayed evidence of DESD (enhanced pelvic floor EMG activity at cystometric capacity) while control rats did not. Only T4 injured rats exhibited evidence of AD, with mean blood pressure elevations from 82.9 +/- 13.6 to 93.9 +/- 11.3 mm Hg ( $P < 0.01$ ) and a mean heart rate decrease from 332.2 +/- 56.5 to 311.1 +/- 54.5 beats/min ( $P = 0.02$ ) at cystometric capacity. The intravenous administration of terazosin or diltiazem abolished the AD response during CMG. The administration of oxybutynin exhibited the ability to increase bladder capacity and improve compliance in all 3 groups but did not blunt AD. The rat model of SCI effectively reproduced hemodynamic changes consistent with the AD complex in T4 level SCI but not T10 level SCI animals, despite incomplete lesions. Blockade with either an alpha-1 or a calcium channel antagonist effectively ablated the AD response to bladder distention. Anticholinergic agents had no effect on AD. DESD frequently accompanies autonomic dysreflexia, although the development of AD is not a prerequisite for DESD.

CONTROLLED TERM: Check Tags: Animal; Comparative Study; Male; Support, Non-U.S. Gov't  
Adrenergic alpha-Antagonists: PD, pharmacology  
\*Autonomic Nervous System Diseases: CO, complications  
\*Autonomic Nervous System Diseases: PP, physiopathology  
Bladder, Neurogenic: DT, drug therapy  
\*Bladder, Neurogenic: PP, physiopathology  
Calcium Channel Blockers: PD, pharmacology  
Diltiazem: PD, pharmacology  
Disease Models, Animal  
Mandelic Acids  
Parasympatholytics: PD, pharmacology  
Prazosin: AA, analogs & derivatives  
Prazosin: PD, pharmacology  
Rats  
Rats, Sprague-Dawley  
\*Spinal Cord Injuries: CO, complications  
Spinal Cord Injuries: DT, drug therapy  
\*Spinal Cord Injuries: PP, physiopathology  
Urodynamics: PH, physiology  
CAS REGISTRY NO.: 19216-56-9 (Prazosin); 42399-41-7 (Diltiazem);

5633-20-5 (oxybutynin); 63590-64-7  
(terazosine)

CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Calcium Channel Blockers); 0 (Mandelic Acids); 0 (Parasympatholytics)

L141 ANSWER 12 OF 31 MEDLINE

ACCESSION NUMBER: 94318991 MEDLINE

DOCUMENT NUMBER: 94318991 PubMed ID: 8043890

TITLE: Clinical reliability of multi-drug intracavernous vasoactive pharmacotherapy for diabetic impotence.

AUTHOR: Montorsi F; Guazzoni G; Bergamaschi F; Zucconi M; Rigatti P; Pizzini G; Miani A; Pozza G

CORPORATE SOURCE: Institute of Human Anatomy, Scientific Institute H. San Raffaele, Milan, Italy.

SOURCE: ACTA DIABETOLOGICA, (1994 Apr) 31 (1) 1-5.

Journal code: 9200299. ISSN: 0940-5429.

PUB. COUNTRY: GERMANY: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199408

ENTRY DATE: Entered STN: 19940909

Last Updated on STN: 19940909

Entered Medline: 19940826

ABSTRACT:

The aim of this study was to assess the effectiveness and safety of intracavernous injections of a four-drug vasoactive mixture in diabetic patients with organic impotence. A group of 60 diabetic patients with either pure neurogenic, pure vasculogenic or mixed neurovasculogenic impotence were treated with intracavernous injections of a combination of 12.1 mg/ml papaverine hydrochloride, 1.01 mg/ml phentolamine mesylate, 10.1 micrograms/ml prostaglandin E1 and 0.15 mg/ml atropine sulphate ('full-dose' mixture). A mixture of the same drugs but at one-third concentrations ('reduced-dose' mixture) was also used. The mean (+/- SEM) volumes of the full-dose and reduced-dose mixtures used were 0.21 +/- 0.03 ml and 0.31 +/- 0.02 ml, respectively. All the patients were able to sustain a rigid erection at the end of the titration phase of the study. At a mean follow-up of 18 months, 48 patients (80%) were successfully using the mixture, 6 patients (10%) were using the mixture at a dose lower than the initial dose and 6 patients (10%) had dropped out from the injection therapy. No major complications were seen. The association of multiple vasoactive drugs which use different mechanisms of action, thus exerting a pharmacological synergism, is an effective and safe procedure in intracavernous pharmacotherapy for diabetic patients with organic impotence.

CONTROLLED TERM: Check Tags: Human; Male

Adult

Aged

Alprostadil: AD, administration & dosage

\*Alprostadil: TU, therapeutic use

Atropine: AD, administration & dosage

\*Atropine: TU, therapeutic use

\*Diabetes Mellitus: CO, complications

Drug Combinations

Follow-Up Studies

\*Impotence: DT, drug therapy

\*Impotence: ET, etiology

Impotence: PP, physiopathology

Injections

Middle Age

Papaverine: AD, administration & dosage

\*Papaverine: TU, therapeutic use

\*Penile Erection: DE, drug effects

Phentolamine: AD, administration & dosage

**\*Phentolamine: TU, therapeutic use**

Self Administration

Treatment Outcome

CAS REGISTRY NO.: 50-60-2 (Phentolamine); 51-55-8 (Atropine); 58-74-2 (Papaverine); 745-65-3 (Alprostadil)

CHEMICAL NAME: 0 (Drug Combinations)

L141 ANSWER 13 OF 31 MEDLINE

ACCESSION NUMBER: 94054844 MEDLINE

DOCUMENT NUMBER: 94054844 PubMed ID: 7694416

TITLE: Effectiveness and safety of multidrug intracavernous therapy for vasculogenic impotence.

AUTHOR: Montorsi F; Guazzoni G; Bergamaschi F; Dodesini A; Rigatti P; Pizzini G; Miani A

CORPORATE SOURCE: Institute of Human Anatomy, Scientific Institut H. San Raffaele, Milan, Italy.

SOURCE: UROLOGY, (1993 Nov) 42 (5) 554-8.  
Journal code: 0366151. ISSN: 0090-4295.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199312

ENTRY DATE: Entered STN: 19940117

Last Updated on STN: 19960129

Entered Medline: 19931207

**ABSTRACT:**

A four-drug vasoactive mixture (papaverine hydrochloride, prostaglandin E1, phentolamine mesylate, atropine sulfate) was used for intracavernous injection therapy in 94 patients with vasculogenic impotence as diagnosed by color Doppler sonography and dynamic infusion cavernosometry-cavernosography. At a mean follow-up of twenty months, 66 patients (70%) are using the injections with the initial dose and are satisfied; 14 patients (15%) are using the injections with a smaller dose than initially given; and 14 patients (15%) dropped intracavernous treatment. Only 4 patients (4%) were unable to achieve a sustained rigid erection during the mixture titration phase. Selected cases of vasculogenic impotence can be safely and effectively treated by the association of drugs which rely on different mechanisms of action, producing a pharmacologic synergism which enhances the overall therapeutic effect.

CONTROLLED TERM: Check Tags: Human; Male

Alprostadil: AD, administration &amp; dosage

**Atropine: AD, administration & dosage**

Drug Synergism

**\*Drug Therapy, Combination**

\*Impotence: DT, drug therapy

Impotence: ET, etiology

Injections, Intravenous

Papaverine: AD, administration &amp; dosage

\*Penis: BS, blood supply

**Phentolamine: AD, administration & dosage****Phentolamine: AA, analogs & derivatives**

CAS REGISTRY NO.: 50-60-2 (Phentolamine); 51-55-8 (Atropine); 58-74-2 (Papaverine); 745-65-3 (Alprostadil)

L141 ANSWER 14 OF 31 MEDLINE

ACCESSION NUMBER: 94167741 MEDLINE

DOCUMENT NUMBER: 94167741 PubMed ID: 7907192

TITLE: Effects of intravesically administered anticholinergics, beta-adrenergic stimulant and alpha-adrenergic blocker on bladder function in unanesthetized rats.

AUTHOR: Ukimura O

CORPORATE SOURCE: Department of Urology, Kyoto Prefectural University of Medicine.

SOURCE: TOHOKU JOURNAL OF EXPERIMENTAL MEDICINE, (1993 Aug) 170 (4)  
251-60.  
Journal code: 0417355. ISSN: 0040-8727.  
PUB. COUNTRY: Japan  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199404  
ENTRY DATE: Entered STN: 19940412  
Last Updated on STN: 19950206  
Entered Medline: 19940405

## ABSTRACT:

Comparative analysis of the effects of intravesical instillation of drugs on urodynamic parameters (MVP, maximum intravesical pressure; RR, residual rate; BC, bladder capacity) was performed using an experimental model in unanesthetized rats. The drugs investigated in this study were atropine ( $7.2 \times 10^{-4}$ - $7.2 \times 10^{-2}$  M), propantheline ( $7.2 \times 10^{-3}$ - $2.2 \times 10^{-2}$  M), \*\*\*oxybutynin\*\*\* ( $2.5 \times 10^{-3}$ - $2.5 \times 10^{-2}$  M), isoproterenol ( $5 \times 10^{-2}$ - $10^{-1}$  M) and prazosin ( $5 \times 10^{-4}$  M). Of the anticholinergics, propantheline and oxybutynin showed a remarkable suppression of MVP accompanied with a consistent increase of RR and BC in a dose-dependent manner. Atropine showed, however, no suppression of MVP in spite of a significant change of RR and BC. Isoproterenol suppressed MVP with an increase of RR and BC in a dose-dependent manner at a relatively high concentration. Prazosin increased BC and RR at a relatively low concentration. This study revealed that these intravesical drugs have the ability to suppress spontaneous bladder contraction in unanesthetized rats and to change the micturition function in the urinary filling and storage phases. It is expected that intravesical instillation therapy for detrusor hyperreflexia will be improved in the future based upon the data obtained.

CONTROLLED TERM: Check Tags: Animal; Male  
Administration, Intravesical  
\*Adrenergic alpha-Antagonists: AD, administration & dosage  
\*Adrenergic beta-Agonists: AD, administration & dosage  
Atropine: AD, administration & dosage  
\*Bladder: DE, drug effects  
Isoproterenol: AD, administration & dosage  
Mandelic Acids: AD, administration & dosage  
\*Parasympatholytics: AD, administration & dosage  
Prazosin: AD, administration & dosage  
Propantheline: AD, administration & dosage  
Rats  
Rats, Wistar

CAS REGISTRY NO.: 19216-56-9 (Prazosin); 298-50-0 (Propantheline);  
51-55-8 (Atropine); 5633-20-5 (oxybutynin);  
7683-59-2 (Isoproterenol)

CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Adrenergic  
beta-Agonists); 0 (Mandelic Acids); 0 (Parasympatholytics)

L141 ANSWER 15 OF 31 MEDLINE

ACCESSION NUMBER: 92173433 MEDLINE

DOCUMENT NUMBER: 92173433 PubMed ID: 1724398

TITLE: Current concepts in the treatment of genitourinary tract  
disorders in the older individual.

AUTHOR: Atala A; Amin M

CORPORATE SOURCE: Department of Surgery, University of Louisville School of  
Medicine, Kentucky.

SOURCE: DRUGS AND AGING, (1991 May) 1 (3) 176-93. Ref: 87  
Journal code: 9102074. ISSN: 1170-229X.

PUB. COUNTRY: New Zealand

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW LITERATURE)

LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199204  
ENTRY DATE: Entered STN: 19920424  
Last Updated on STN: 19960129  
Entered Medline: 19920408

## ABSTRACT:

Genitourinary problems, including neurogenic dysfunction, impotence, prostatism, urinary tract infections, and prostate cancer, are common in the elderly, and most of the symptoms can be alleviated through pharmacological management. Patients with neurogenic dysfunction who present with symptoms such as incontinence and urinary retention can be appropriately managed with bladder and sphincter relaxants or stimulants. Anticholinergic agents in the form of **oxybutynin**, flavoxate, and propantheline are effective bladder relaxants, and phenoxybenzamine, prazosin, and **terazosin** are commonly used as sphincter relaxants. Bethanechol chloride is the agent most commonly used to stimulate bladder contraction, but physicians should be careful when prescribing it for elderly patients with cardiovascular problems. Organic and psychogenic causes of impotence usually overlap, and oral agents have limited use in the treatment process. The use of yohimbine has increased recently, but its value and rate of success remains questionable. Testosterone is being used widely to treat impotence, but it is only helpful to patients with hypogonadism and should be used with discretion in the elderly, who have a high incidence of prostate cancer. Vasoactive intracavernous pharmacotherapy, on the other hand, is a recently discovered alternative to testosterone with promising results. Although the treatment of choice for benign prostatic hypertrophy is surgery, there have been important pharmacological advances in treating this disorder. alpha-Adrenergic antagonists and anti-androgenic agents have been found to relieve the symptoms of prostatic enlargement. The use of chemotherapeutic and antibiotic agents to treat and suppress acute and chronic urinary tract infections is reviewed; these are second only to pulmonary infections as the most frequent cause of febrile episodes in patients over the age of 65. Lower urinary tract infections can be treated with almost any antibacterial agent. Upper urinary tract infections require full genitourinary evaluation and appropriate antibiotics should be used according to the urine culture sensitivity studies. With the advent of new hormonal agents, more choices are now available for the management of prostate cancer, which is the second most common malignancy in men. Diethylstilbestrol (stilboestrol), an oral estrogen, remains a commonly used agent to achieve castrate levels of androgens in advanced prostatic carcinoma. Agonist analogues, such as goserelin and leuprorelin, of gonadotrophin-releasing hormone (GnRH) [luteinising hormone-releasing hormone (LHRH); or gonadorelin] achieve the same results as diethylstilbestrol but without the cardiovascular side effects. Antiandrogens are also being used in combination with GnRH agonists to produce complete androgen blockage, with mixed results.

CONTROLLED TERM: Check Tags: Human; Male  
Aged  
Impotence: DT, drug therapy  
Prostatic Hyperplasia: DT, drug therapy  
Prostatic Neoplasms: DT, drug therapy  
Urinary Tract Infections: DT, drug therapy  
\*Urogenital Diseases: DT, drug therapy

L141 ANSWER 16 OF 31 MEDLINE  
ACCESSION NUMBER: 88129771 MEDLINE  
DOCUMENT NUMBER: 88129771 PubMed ID: 2963479  
TITLE: The effects of thymoxamine, phenylephrine and cyclopentolate on the accommodative process in man.  
Zetterstrom C  
AUTHOR: Department of Ophthalmology, Hospital of Uppsala, Sweden.  
CORPORATE SOURCE: ACTA OPHTHALMOLOGICA, (1987 Dec) 65 (6) 699-704.  
SOURCE: Journal code: 0370347. ISSN: 0001-639X.  
PUB. COUNTRY: Denmark

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198803  
ENTRY DATE: Entered STN: 19900308  
Last Updated on STN: 19900308  
Entered Medline: 19880314

## ABSTRACT:

Accommodation of the eye was measured in a cross-over study in 11 healthy volunteers (20-35 years). In 5 subjects the near point was determined before and after topical instillation of 5 microliter of 0.1% and 0.5%, and 5 x 5 microliter 0.5% thymoxamine, 5 microliter of 2% and 10%, and 5 x 5 microliter 10% phenylephrine and 5 microliter of 0.04%, 0.2%, and 1% cyclopentolate. All concentrations of thymoxamine increased the accommodative amplitude by about 1.5 dioptres. Accommodation decreased by about 0.5 dioptre after instillation of 5 x 5 microliter 10% phenylephrine. The cycloplegic effects of 0.2% and 1% cyclopentolate were similar. Accommodation was also determined after application of 5 microliter 1% cyclopentolate followed by either 5 x 5 microliter 0.5% thymoxamine or 10% phenylephrine. Addition of thymoxamine did not alter the cycloplegic response of cyclopentolate alone. Addition of phenylephrine caused a more prolonged but similar maximum response compared to that of cyclopentolate alone. In the 6 other test subjects, the accommodation was compared before and after topical instillation of 5 microliter of 0.2% and 1% and 40 microliter (one standard eye-drop) of 1% cyclopentolate and followed during 6 h. There was no difference between the maximum value of 5 microliter and 40 microliter 1% cyclopentolate. We conclude from these data that alpha-stimulation by phenylephrine decreases and alpha-inhibition by thymoxamine increases the accommodative amplitude in man. (ABSTRACT TRUNCATED AT 250 WORDS)

CONTROLLED TERM: Check Tags: Human  
\*Accommodation, Ocular: DE, drug effects  
Adult  
Ciliary Body: DE, drug effects  
\*Cyclopentolate: PD, pharmacology  
Drug Combinations  
\*Moxisylyte: PD, pharmacology

\*Phenylacetates: PD, pharmacology  
\*Phenylephrine: PD, pharmacology  
CAS REGISTRY NO.: 512-15-2 (Cyclopentolate); 54-32-0 (Moxisylyte); 59-42-7 (Phenylephrine)

CHEMICAL NAME: 0 (Drug Combinations); 0 (Phenylacetates)

L141 ANSWER 17 OF 31 MEDLINE

ACCESSION NUMBER: 85306123 MEDLINE  
DOCUMENT NUMBER: 85306123 PubMed ID: 3929733  
TITLE: [Chemical blockade of the cardiac autonomic nervous system. Effects on the coronary arterial vasomotor activity].  
Blocage chimique du système nerveux autonome cardiaque.  
Effets sur la vasomotricité artérielle coronaire.  
AUTHOR: Bory M; Dayan-Benattar N; Sainsous J; Djiane P; Serradimigni A  
SOURCE: ARCHIVES DES MALADIES DU COEUR ET DES VAISSEAUX, (1985 Jul) 78 (7) 1053-60.  
Journal code: 0406011. ISSN: 0003-9683.  
PUB. COUNTRY: France  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: French  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198510  
ENTRY DATE: Entered STN: 19900320  
Last Updated on STN: 19900320  
Entered Medline: 19851021  
ABSTRACT:

The results of cardiac plexectomy in spastic angina are controversial. This study was undertaken to evaluate the effects of blocking the cardiac autonomic nervous system (CANS) in this syndrome in 61 patients presenting with chest pain and angiographically normal coronary arteries. All patients underwent a methyl-ergometrine provocation test with a sequential protocol. They were then divided into two groups: Group 1 (13 patients): positive response to ergometrine. Group 2 (48 patients): negative response to ergometrine. Three sub-groups were identified: 2: 1: 9 patients with coronary spasm demonstrated by another method: 2: 2: 6 patients with myocardial infarction: 2: 3: 33 patients with chest pain alone. The results of these tests were compared with those obtained after blocking the CANS by intravenous injection over 3 minutes of an alpha and beta-blocker (labetalol 2 mg/kg) and a parasympathetic blocker (Atropine. 0.04 mg/kg). The CANS blockade was confirmed by two facts: the basal heart rate of  $66.38 \pm 9.91$  rose to its intrinsic rate of  $89.76 \pm 10.5$  (p less than 0.01) and remained at that rate after ergometrine and trinitrate administration and myocardial ischaemia; changes in blood pressure were greater after CANS blockade:  $+30.62 \pm 16.13$  mmHg instead of  $+8.62 \pm 0.33$  mmHg after ergometrine (p less than 0.01) and  $-43.16 \pm 16.32$  mmHg instead of  $-25.16 \pm 3.64$  mmHg after trinitrate (p less than 0.01). (ABSTRACT TRUNCATED AT 250 WORDS)

CONTROLLED TERM: Check Tags: Female; Human; Male

Adult

Aged

\*Atropine: TU, therapeutic use

\*Autonomic Nerve Block

Blood Pressure: DE, drug effects

\*Coronary Vasospasm: DT, drug therapy

Drug Therapy, Combination

Electrocardiography

English Abstract

\*Ethanalamines: TU, therapeutic use

\*Heart: IR, innervation

Heart: RI, radionuclide imaging

Heart Rate: DE, drug effects

\*Labetalol: TU, therapeutic use

Middle Age

CAS REGISTRY NO.: 36894-69-6 (Labetalol); 51-55-8 (Atropine)

CHEMICAL NAME: 0 (Ethanalamines)

L141 ANSWER 18 OF 31

MEDLINE

ACCESSION NUMBER: 84002050 MEDLINE

DOCUMENT NUMBER: 84002050 PubMed ID: 6137279

TITLE: Treatment of vasospastic angina.

AUTHOR:

MacAlpin R

SOURCE: CARDIOVASCULAR CLINICS, (1983) 14 (1) 129-72. Ref: 255

Journal code: 0213744. ISSN: 0069-0384.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198311

ENTRY DATE: Entered STN: 19900319

Last Updated on STN: 19950206

Entered Medline: 19831123

CONTROLLED TERM: Check Tags: Case Report; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.

Adrenergic alpha-Antagonists: TU, therapeutic use

Adrenergic beta-Antagonists: TU, therapeutic use

Adult

Anemia: CO, complications

Angina Pectoris, Variant: CO, complications

\*Angina Pectoris, Variant: DT, drug therapy

Atropine: TU, therapeutic use  
Diltiazem: TU, therapeutic use  
Drug Therapy, Combination  
Epoprostenol: TU, therapeutic use  
Exercise Therapy  
Hypertension: CO, complications  
Hyperthyroidism: CO, complications  
Isosorbide Dinitrate: TU, therapeutic use  
Middle Age  
Nifedipine: TU, therapeutic use  
Nitroglycerin: TU, therapeutic use  
Nitroprusside: TU, therapeutic use  
Nylidrin: TU, therapeutic use  
Verapamil: TU, therapeutic use

CAS REGISTRY NO.: 15078-28-1 (Nitroprusside); 21829-25-4 (Nifedipine);  
35121-78-9 (Epoprostenol); 42399-41-7 (Diltiazem); 447-41-6  
(Nylidrin); 51-55-8 (Atropine); 52-53-9 (Verapamil);  
55-63-0 (Nitroglycerin); 87-33-2 (Isosorbide Dinitrate)  
CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Adrenergic  
beta-Antagonists)

L141 ANSWER 19 OF 31 MEDLINE  
ACCESSION NUMBER: 83051350 MEDLINE  
DOCUMENT NUMBER: 83051350 PubMed ID: 6814784  
TITLE: Antiarrhythmic drug combinations in the treatment of  
ventricular tachycardia.  
AUTHOR: Ross D L; Sze D Y; Keefe D L; Swerdlow C D; Echt D S;  
Griffin J C; Winkle R A; Mason J W  
SOURCE: CIRCULATION, (1982 Dec) 66 (6) 1205-10.  
Journal code: 0147763. ISSN: 0009-7322.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 198301  
ENTRY DATE: Entered STN: 19900317  
Last Updated on STN: 19900317  
Entered Medline: 19830107

## ABSTRACT:

Combinations of antiarrhythmic drugs are frequently used to treat refractory ventricular tachycardia (VT), but few scientific data support this practice. We examined the efficacy and electrophysiology of 110 antiarrhythmic drug combination trials at electrophysiologic study in 74 patients with recurrent ventricular tachycardia. Lidocaine was combined with quinidine in 33 trials, procainamide in 22 and encainide in 20. Propranolol was combined with quinidine in 17 trials, procainamide in 12 and encainide in six. All individual drugs tested (except propranolol, which was usually not tested individually) had failed at electrophysiologic study or clinically in the presence of usually accepted plasma concentrations. Lidocaine in combination with quinidine was effective in 3% of the trials, with procainamide in 5% and with encainide in none of the trials. Propranolol in combination with quinidine was effective in 18% of the trials, with procainamide in 17% and with encainide in none of the trials. The electrophysiologic effects of the tested drug combinations were dominated by the individual effects of the type 1 antiarrhythmic agents. We conclude that the tested antiarrhythmic drug combinations are infrequently effective in preventing VT induction at electrophysiologic study when each agent has failed individually. The addition of lidocaine or propranolol to quinidine, procainamide or encainide does not produce significant synergistic or new effects on the electrophysiologic variables analyzed.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't  
Aged  
Anilides: BL, blood

Anilides: TU, therapeutic use  
Anti-Arrhythmia Agents: AE, adverse effects  
Anti-Arrhythmia Agents: BL, blood  
\*Anti-Arrhythmia Agents: TU, therapeutic use  
Blood Pressure: DE, drug effects  
\*Drug Therapy, Combination  
Electrophysiology  
Encainide  
Lidocaine: AA, analogs & derivatives  
Lidocaine: BL, blood  
Lidocaine: TU, therapeutic use  
Middle Age  
Procainamide: BL, blood  
Procainamide: TU, therapeutic use  
Propranolol: AE, adverse effects  
Propranolol: TU, therapeutic use  
Quinidine: BL, blood  
Quinidine: TU, therapeutic use  
\*Tachycardia: DT, drug therapy  
Tachycardia: PP, physiopathology  
Tocainide

CAS REGISTRY NO.: 137-58-6 (Lidocaine); 41708-72-9 (Tocainide); 51-06-9  
(Procainamide); 525-66-6 (Propranolol); 56-54-2  
(Quinidine); 66778-36-7 (Encainide)  
CHEMICAL NAME: 0 (Anilides); 0 (Anti-Arrhythmia Agents)

L141 ANSWER 20 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2003036185 EMBASE

TITLE: As we enter the new year, several new drugs will be  
launched globally.

AUTHOR: Wyllie M.G.

CORPORATE SOURCE: Dr. M.G. Wyllie, Urodoc, Herne Bay, Kent, United Kingdom.  
mike@urodoc.co.uk

SOURCE: BJU International, (2003) 91/1 (115-116).  
ISSN: 1464-4096 CODEN: BJINFO

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; (Short Survey)

FILE SEGMENT: 028 Urology and Nephrology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:  
\*prostate hypertrophy: DT, drug therapy  
erectile dysfunction: DT, drug therapy  
urge incontinence: DT, drug therapy  
food and drug administration  
urine retention  
health care  
economic aspect  
long term care  
treatment outcome  
drug efficacy  
cardiovascular effect  
side effect: SI, side effect  
patient compliance  
human  
short survey  
priority journal  
Drug Descriptors:  
\*new drug  
sildenafil: AE, adverse drug reaction

sildenafil: DT, drug therapy  
sildenafil: PD, pharmacology  
phosphodiesterase inhibitor  
vardenafil  
tadalafil  
darifenacin: DT, drug therapy  
solifenacin: DT, drug therapy  
steroid 5alpha reductase: CB, drug combination  
steroid 5alpha reductase: DT, drug therapy  
**alpha adrenergic receptor blocking agent: CB, drug combination**  
alpha adrenergic receptor blocking agent: DT, drug therapy  
steroid 5alpha reductase inhibitor: DT, drug therapy  
dutasteride: AE, adverse drug reaction  
dutasteride: DT, drug therapy  
dutasteride: PD, pharmacology  
finasteride: AE, adverse drug reaction  
finasteride: DT, drug therapy  
androgen: EC, endogenous compound  
fiduxosin: DT, drug therapy  
adrenergic receptor blocking agent: CB, drug combination  
adrenergic receptor blocking agent: DT, drug therapy  
parvosin: DT, drug therapy  
tamsulosin: DT, drug therapy  
oxybutynin: DT, drug therapy  
tolterodine: DT, drug therapy  
**muscarinic receptor blocking agent: CB, drug combination**  
muscarinic receptor blocking agent: DT, drug therapy  
dopamine receptor stimulating agent: AE, adverse drug reaction  
dopamine receptor stimulating agent: DT, drug therapy  
dopamine receptor stimulating agent: LI, sublingual drug administration  
apomorphine: AE, adverse drug reaction  
apomorphine: DT, drug therapy  
apomorphine: LI, sublingual drug administration  
phentolamine: DT, drug therapy  
unclassified drug  
rxs 70004  
uk 380003  
rbx 2258  
CAS REGISTRY NO.: (sildenafil) 139755-83-2; (vardenafil) 224785-90-4,  
224785-91-5, 224789-15-5; (tadalafil) 171596-29-5;  
(darifenacin) 133099-04-4, 133099-07-7; (solifenacin)  
180272-14-4, 180272-16-6, 180468-39-7; (dutasteride)  
164656-23-9; (finasteride) 98319-26-7; (fiduxosin)  
208992-74-9; (tamsulosin) 106133-20-4, 106138-88-9,  
106463-17-6, 80223-99-0, 94666-07-6; (oxybutynin)  
1508-65-2, 5633-20-5; (tolterodine) 124937-51-5;  
(apomorphine) 314-19-2, 58-00-4; (phentolamine) 50-60-2,  
73-05-2  
CHEMICAL NAME: (1) Rxs 70004; (2) Uk 380003; (3) Rbx 2258  
COMPANY NAME: (1) Hoffmann La Roche; (2) Pfizer; (3) Schwarz; Lilly;  
Yamanouchi; Abbott; Bayer; Ortho

L141 ANSWER 21 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 2003124545 EMBASE  
TITLE: Efficacy and safety of tolterodine in subjects with  
symptoms of overactive bladder: An open label,  
noncomparative, prospective, multicentric study.  
AUTHOR: Kumar A.  
CORPORATE SOURCE: Prof. A. Kumar, Dept. of Urol. and Renal Transplant.,

SOURCE: SGP GIMS, Rai Bareilly Road, Lucknow 226 014, India  
Indian Journal of Urology, (2002) 19/1 (73-78).  
Refs: 14  
ISSN: 0970-1591 CODEN: IJURE2

COUNTRY: India

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 028 Urology and Nephrology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Objective: To evaluate the clinical efficacy and safety of tolterodine 2 mg twice daily in Indian subjects with symptoms of overactive bladder including frequency, urgency with or without urge incontinence. Methods: This multicentric open-label, noncomparative, prospective study was conducted at 7 centers across India. Eligible patients were assigned to treatment with Tab. Tolterodine 2 mg twice daily for 8 weeks. Subjects were seen at visit 1 (day 3 to 10), visit 2 (day 1) and after 8 weeks of treatment. Micturition charts were completed prior to visit 2 and visit 3. Efficacy variables included change from baseline to 8 weeks of treatment in the mean number of micturitions, incontinence episodes/24 hours, mean volume voided per micturition and subjects' perception of treatment benefit. Efficacy was evaluated from patients' micturition diaries. Patients were also assessed for adverse events during the treatment. Results: A total of 127 subjects with symptoms of overactive bladder were enrolled. 8 weeks' treatment with tolterodine resulted in improvement in assessment of all symptoms of overactive bladder. Significant decreases from baseline in both the frequency of micturition (mean  $\pm$  SD of  $-2.5 \pm 5.0$  per 24 hours,  $p=0.0001$ ) and the number of incontinence episodes per 24 hours ( $-1.5 \pm 3.8$ ,  $p=0.0051$ ) and a significant increase in mean volume voided per micturition ( $+26 \pm 55$  ml,  $p=0.0001$ ) were obtained. Treatment was well tolerated and most subjects (71.4%) did not experience any adverse events during the study. The most common adverse event was dry mouth (10.3%). 5 subjects were withdrawn due to adverse events and all the subjects recovered uneventfully. Conclusions: Treatment with Tolterodine 2 mg twice daily was effective and safe in Indian subjects with the symptoms of overactive bladder, as assessed by both objective and subjective criteria.

CONTROLLED TERM: Medical Descriptors:  
\*overactive bladder: DT, drug therapy  
human  
major clinical study  
multicenter study  
clinical trial  
adult  
aged  
female  
male  
drug efficacy  
drug safety  
open study  
prospective study  
drug dose regimen  
Indian  
urge incontinence: DT, drug therapy  
consultation  
micturition  
urine volume  
drug tolerability  
side effect: SI, side effect  
xerostomia: SI, side effect  
disease duration

urine incontinence: DT, drug therapy  
autonomic dysfunction: SI, side effect  
central nervous system disease: SI, side effect  
peripheral neuropathy: SI, side effect  
urine retention: SI, side effect  
drug fever: SI, side effect  
drug withdrawal  
anxiety  
paresthesia: SI, side effect  
hypokinesia: SI, side effect  
enzyme blood level  
hematuria: SI, side effect  
urinary tract infection: SI, side effect  
leukocyte count  
leukopenia: SI, side effect  
gastrointestinal symptom: SI, side effect  
hearing disorder: SI, side effect  
vestibular disorder: SI, side effect  
liver disease: SI, side effect  
biliary tract disease: SI, side effect  
metabolic disorder: SI, side effect  
nutritional disorder: SI, side effect  
musculoskeletal disease: SI, side effect  
mental disease: SI, side effect  
respiratory tract disease: SI, side effect  
skin disease: SI, side effect  
India  
patient attitude  
medical record  
urinary frequency  
perception  
liver dysfunction: SI, side effect  
article

Drug Descriptors:

\*tolterodine: DT, drug therapy  
\*tolterodine: CT, clinical trial  
\*tolterodine: PO, oral drug administration  
\*tolterodine: PD, pharmacology  
\*tolterodine: AE, adverse drug reaction

**\*tolterodine: CB, drug combination**

oxybutynin: DT, drug therapy  
oxybutynin: AE, adverse drug reaction  
amlodipine: DT, drug therapy  
amlodipine: CB, drug combination  
atenolol: DT, drug therapy  
atenolol: CB, drug combination  
nifedipine: DT, drug therapy  
nifedipine: CB, drug combination  
doxazosin: DT, drug therapy

**doxazosin: CB, drug combination**

paracetamol: DT, drug therapy  
paracetamol: CB, drug combination  
liver enzyme: EC, endogenous compound

CAS REGISTRY NO.: (tolterodine) 124937-51-5; (oxybutynin) 1508-65-2,  
5633-20-5; (amlodipine) 88150-42-9; (atenolol) 29122-68-7;  
(nifedipine) 21829-25-4; (doxazosin) 74191-85-8;  
(paracetamol) 103-90-2

L141 ANSWER 22 OF 31. EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001083847 EMBASE

TITLE: A review of the treatment options for clozapine-induced  
hypersalivation.

AUTHOR: Cree A.; Mir S.; Fahy T.

CORPORATE SOURCE: A. Cree, Maudsley Hospital, Denmark Hill, London SE5 8AF,  
United Kingdom

SOURCE: Psychiatric Bulletin, (2001) 25/3 (114-116).  
Refs: 17

ISSN: 0955-6036 CODEN: PBULE5

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 038 Adverse Reactions Titles  
011 Otorhinolaryngology  
032 Psychiatry  
037 Drug Literature Index  
030 Pharmacology  
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Aims and method: To develop and introduce an evidence-based drug treatment protocol for clozapine-induced hypersalivation, a review of published literature relating to clozapine-induced hypersalivation and its treatment was undertaken in March 2000. The databases searched were Medline, EMBASE and PsychLit, from 1966 to the present. Results: This paper reviews the evidence of the benefit of using antimuscarinic agents, adrenergic antagonists and adrenergic agonists. There is a lack of good-quality controlled-trials, with most papers reporting a series of uncontrolled cases dependent on subjective measures of improvement reported by the patients. However, the published literature suggests a benefit for all of the drug categories reviewed. The most effective treatment may be a combination of terazosin and benzhexol. Clinical implications: Clozapine-induced hypersalivation is not only an embarrassing problem, but can be difficult to treat. An evidence-based prescribing protocol will encourage the use of those drugs found to be the most effective in treating this problem. It will also offer alternatives if a certain treatment is ineffective or intolerable.

CONTROLLED TERM: Medical Descriptors:  
\*hypersalivation: SI, side effect  
\*hypersalivation: DT, drug therapy  
\*hypersalivation: TH, therapy  
human  
clinical trial  
drug efficacy  
evidence based medicine  
drug tolerability  
drug mechanism  
receptor blocking  
dose response  
receptor affinity  
depression: SI, side effect  
xerostomia: SI, side effect  
visual impairment: SI, side effect  
diarrhea: SI, side effect  
drug penetration  
hypotension: SI, side effect  
confusion: SI, side effect  
schizophrenia: DT, drug therapy  
drug response  
drug absorption  
bradycardia: SI, side effect  
contact dermatitis: SI, side effect  
psychosis: SI, side effect  
swallowing  
diet therapy  
review  
Drug Descriptors:

\*clozapine: AE, adverse drug reaction  
\*clozapine: PD, pharmacology  
\*clozapine: CT, clinical trial  
\*clozapine: DO, drug dose  
\*muscarinic receptor blocking agent: DT, drug therapy  
\*muscarinic receptor blocking agent: CT, clinical trial  
\*muscarinic receptor blocking agent: PD, pharmacology  
\*muscarinic receptor blocking agent: DO, drug dose  
\*muscarinic receptor blocking agent: AE, adverse drug reaction  
\*muscarinic receptor blocking agent: PK, pharmacokinetics  
\*muscarinic receptor blocking agent: CM, drug comparison  
\*muscarinic receptor blocking agent: LI, sublingual drug administration  
\*muscarinic receptor blocking agent: NA, intranasal drug administration  
\*muscarinic receptor blocking agent: CB, drug combination  
\*adrenergic receptor blocking agent: DT, drug therapy  
\*adrenergic receptor blocking agent: CT, clinical trial  
\*adrenergic receptor blocking agent: PD, pharmacology  
\*adrenergic receptor blocking agent: CB, drug combination  
\*adrenergic receptor blocking agent: AE, adverse drug reaction  
\*adrenergic receptor blocking agent: CM, drug comparison  
\*adrenergic receptor blocking agent: DO, drug dose  
\*adrenergic receptor stimulating agent: DT, drug therapy  
\*adrenergic receptor stimulating agent: CT, clinical trial  
\*adrenergic receptor stimulating agent: PD, pharmacology  
\*adrenergic receptor stimulating agent: DO, drug dose  
\*adrenergic receptor stimulating agent: AE, adverse drug reaction  
terazosin: DT, drug therapy  
terazosin: CB, drug combination  
terazosin: PD, pharmacology  
terazosin: AE, adverse drug reaction  
terazosin: CM, drug comparison  
terazosin: CT, clinical trial  
terazosin: DO, drug dose  
trihexyphenidyl: DT, drug therapy  
trihexyphenidyl: CB, drug combination  
trihexyphenidyl: PD, pharmacology  
trihexyphenidyl: PK, pharmacokinetics  
trihexyphenidyl: AE, adverse drug reaction  
trihexyphenidyl: DO, drug dose  
trihexyphenidyl: CM, drug comparison  
muscarinic receptor: EC, endogenous compound  
adrenergic receptor: EC, endogenous compound  
amitriptyline: DT, drug therapy  
amitriptyline: PD, pharmacology  
amitriptyline: DO, drug dose  
pirenzepine: DT, drug therapy  
pirenzepine: PD, pharmacology  
pirenzepine: AE, adverse drug reaction  
pirenzepine: DO, drug dose  
benzatropine: DT, drug therapy  
benzatropine: PD, pharmacology  
benzatropine: CM, drug comparison  
benzatropine: AE, adverse drug reaction  
benzatropine: DO, drug dose  
benzatropine: CT, clinical trial  
benzatropine: CB, drug combination  
atropine: DT, drug therapy

atropine: PD, pharmacology  
atropine: AE, adverse drug reaction  
atropine: LI, sublingual drug administration  
atropine: DO, drug dose  
scopolamine bromide: DT, drug therapy  
scopolamine bromide: PD, pharmacology  
ipratropium bromide: DT, drug therapy  
ipratropium bromide: PD, pharmacology  
ipratropium bromide: NA, intranasal drug administration  
ipratropium bromide: PK, pharmacokinetics  
ipratropium bromide: AE, adverse drug reaction  
ipratropium bromide: CT, clinical trial  
clonidine: DT, drug therapy  
clonidine: PD, pharmacology  
clonidine: DO, drug dose  
clonidine: AE, adverse drug reaction  
lofexidine: DT, drug therapy  
lofexidine: PD, pharmacology  
lofexidine: DO, drug dose  
lofexidine: AE, adverse drug reaction  
CAS REGISTRY NO.: (clozapine) 5786-21-0; (terazosin) 63074-08-8, 63590-64-7;  
(trihexyphenidyl) 144-11-6, 52-49-3; (amitriptyline)  
50-48-6, 549-18-8; (pirenzepine) 28797-61-7, 29868-97-1;  
(benzatropine) 86-13-5; (atropine) 51-55-8, 55-48-1;  
(scopolamine bromide) 114-49-8; (ipratropium bromide)  
22254-24-6; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8;  
(lofexidine) 31036-80-3

L141 ANSWER 23 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 2000081881 EMBASE  
TITLE: Pharmacologic management of urinary incontinence.  
AUTHOR: Lackner T.E.  
CORPORATE SOURCE: Dr. T.E. Lackner, College of Pharmacy, Weaver-Densford  
Hall, University of Minnesota, 308 Harvard St SE,  
Minneapolis, MN 55455, United States. lackn001@tc.umn.edu  
SOURCE: Annals of Long-Term Care, (2000) 8/2 (29-37).  
Refs: 30  
ISSN: 1524-7929 CODEN: ALTCTF  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 020 Gerontology and Geriatrics  
028 Urology and Nephrology  
036 Health Policy, Economics and Management  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ABSTRACT:

Urinary incontinence, overactive bladder without incontinence, and their complications are widespread. They constitute an important cause of medical, psychosocial, and hygienic problems and an economic burden in the long-term care population. Treatment of urinary incontinence/overactive bladder can significantly relieve symptoms, with complete continence restored in some patients. As an adjunct to nonpharmacologic therapies, new drugs are associated with a lower risk of adverse drug reactions, improved patient tolerance, and greater convenience than traditional agents and may enable a greater number of patients to realize improved bladder control.

CONTROLLED TERM: Medical Descriptors:  
\*urine incontinence: DM, disease management  
\*urine incontinence: DT, drug therapy  
\*urine incontinence: ET, etiology  
\*urine incontinence: TH, therapy

\*stress incontinence: DM, disease management  
\*stress incontinence: DT, drug therapy  
\*stress incontinence: ET, etiology  
\*stress incontinence: TH, therapy  
incontinence: DM, disease management  
incontinence: DT, drug therapy  
incontinence: ET, etiology  
incontinence: TH, therapy  
geriatric patient  
detrusor muscle  
    **bladder contraction**  
drug metabolism  
drug effect  
drug induced disease: SI, side effect  
drug cost  
human  
aged  
review  
Drug Descriptors:  
\*cholinergic receptor blocking agent: AE, adverse drug  
reaction  
\*cholinergic receptor blocking agent: DO, drug dose  
\*cholinergic receptor blocking agent: IT, drug interaction  
\*cholinergic receptor blocking agent: DT, drug therapy  
\*cholinergic receptor blocking agent: PR, pharmaceuticals  
\*cholinergic receptor blocking agent: PK, pharmacokinetics  
\*cholinergic receptor blocking agent: PO, oral drug  
administration  
\*tolterodine: AE, adverse drug reaction  
\*tolterodine: DO, drug dose  
    **\*tolterodine: IT, drug interaction**  
\*tolterodine: DT, drug therapy  
\*tolterodine: PE, pharmacoeconomics  
\*tolterodine: PK, pharmacokinetics  
\*tolterodine: PO, oral drug administration  
\*cholinergic receptor stimulating agent: AE, adverse drug  
reaction  
\*cholinergic receptor stimulating agent: DO, drug dose  
\*cholinergic receptor stimulating agent: IT, drug  
interaction  
\*cholinergic receptor stimulating agent: DT, drug therapy  
\*cholinergic receptor stimulating agent: PE,  
pharmacoeconomics  
\*cholinergic receptor stimulating agent: PO, oral drug  
administration  
\*cholinergic receptor stimulating agent: SC, subcutaneous  
drug administration  
\*bethanechol: AE, adverse drug reaction  
\*bethanechol: DO, drug dose  
\*bethanechol: IT, drug interaction  
\*bethanechol: DT, drug therapy  
\*bethanechol: PE, pharmacoeconomics  
\*bethanechol: PO, oral drug administration  
\*bethanechol: SC, subcutaneous drug administration  
\*alpha adrenergic receptor stimulating agent: AE, adverse  
drug reaction  
\*alpha adrenergic receptor stimulating agent: DO, drug dose  
\*alpha adrenergic receptor stimulating agent: IT, drug  
interaction  
\*alpha adrenergic receptor stimulating agent: DT, drug  
therapy  
\*alpha adrenergic receptor stimulating agent: PE,  
pharmacoeconomics

\*alpha adrenergic receptor stimulating agent: PO, oral drug administration  
\*alpha 1 adrenergic receptor blocking agent: AE, adverse drug reaction  
\*alpha 1 adrenergic receptor blocking agent: DO, drug dose  
\*alpha 1 adrenergic receptor blocking agent: IT, drug interaction  
\*alpha 1 adrenergic receptor blocking agent: DT, drug therapy  
\*alpha 1 adrenergic receptor blocking agent: PE, pharmacoeconomics  
\*alpha 1 adrenergic receptor blocking agent: PO, oral drug administration  
\*tricyclic antidepressant agent: AE, adverse drug reaction  
\*tricyclic antidepressant agent: DO, drug dose  
\*tricyclic antidepressant agent: IT, drug interaction  
\*tricyclic antidepressant agent: DT, drug therapy  
\*tricyclic antidepressant agent: PE, pharmacoeconomics  
\*tricyclic antidepressant agent: PO, oral drug administration  
estrogen: AE, adverse drug reaction  
estrogen: DT, drug therapy  
estrogen: PE, pharmacoeconomics  
estrogen: VA, intravaginal drug administration  
estrogen: DL, intradermal drug administration  
antiestrogen: AE, adverse drug reaction  
antiestrogen: DT, drug therapy  
antiestrogen: PE, pharmacoeconomics  
antiestrogen: PO, oral drug administration  
finasteride: AE, adverse drug reaction  
finasteride: DT, drug therapy  
finasteride: PE, pharmacoeconomics  
finasteride: PO, oral drug administration  
doxazosin: AE, adverse drug reaction  
doxazosin: DO, drug dose  
**doxazosin: IT, drug interaction**  
doxazosin: DT, drug therapy  
doxazosin: PE, pharmacoeconomics  
doxazosin: PO, oral drug administration  
tamsulosin: AE, adverse drug reaction  
tamsulosin: DO, drug dose  
tamsulosin: IT, drug interaction  
tamsulosin: DT, drug therapy  
tamsulosin: PE, pharmacoeconomics  
tamsulosin: PO, oral drug administration  
terazosin: AE, adverse drug reaction  
terazosin: DO, drug dose  
**terazosin: IT, drug interaction**  
terazosin: DT, drug therapy  
terazosin: PE, pharmacoeconomics  
terazosin: PO, oral drug administration  
oxybutynin: AE, adverse drug reaction  
oxybutynin: DO, drug dose  
**oxybutynin: IT, drug interaction**  
oxybutynin: DT, drug therapy  
oxybutynin: PE, pharmacoeconomics  
oxybutynin: PO, oral drug administration  
propantheline bromide: AE, adverse drug reaction  
propantheline bromide: DO, drug dose  
propantheline bromide: IT, drug interaction  
propantheline bromide: DT, drug therapy  
propantheline bromide: PE, pharmacoeconomics  
propantheline bromide: PO, oral drug administration

phenylpropanolamine: AE, adverse drug reaction  
phenylpropanolamine: DO, drug dose  
phenylpropanolamine: IT, drug interaction  
phenylpropanolamine: DT, drug therapy  
phenylpropanolamine: PE, pharmacoeconomics  
phenylpropanolamine: PO, oral drug administration  
pseudoephedrine: AE, adverse drug reaction  
pseudoephedrine: DO, drug dose  
pseudoephedrine: IT, drug interaction  
pseudoephedrine: DT, drug therapy  
pseudoephedrine: PE, pharmacoeconomics  
pseudoephedrine: PO, oral drug administration  
Sabal extract: AE, adverse drug reaction  
Sabal extract: DT, drug therapy  
Sabal extract: PE, pharmacoeconomics  
desipramine: AE, adverse drug reaction  
desipramine: DO, drug dose  
desipramine: IT, drug interaction  
desipramine: DT, drug therapy  
desipramine: PE, pharmacoeconomics  
desipramine: PO, oral drug administration  
doxepin: AE, adverse drug reaction  
doxepin: DO, drug dose  
doxepin: IT, drug interaction  
doxepin: DT, drug therapy  
doxepin: PE, pharmacoeconomics  
doxepin: PO, oral drug administration  
imipramine: AE, adverse drug reaction  
imipramine: DO, drug dose  
imipramine: IT, drug interaction  
imipramine: DT, drug therapy  
imipramine: PE, pharmacoeconomics  
imipramine: PO, oral drug administration  
nortriptyline: AE, adverse drug reaction  
nortriptyline: DO, drug dose  
nortriptyline: IT, drug interaction  
nortriptyline: DT, drug therapy  
nortriptyline: PE, pharmacoeconomics  
nortriptyline: PO, oral drug administration  
antihypertensive agent: IT, drug interaction  
theophylline: IT, drug interaction  
steroid: IT, drug interaction  
monoamine oxidase inhibitor: IT, drug interaction  
antibiotic agent: IT, drug interaction  
cannabinoid: IT, drug interaction  
antifungal agent: IT, drug interaction  
unindexed drug

CAS REGISTRY NO.: (tolterodine) 124937-51-5; (bethanechol) 590-63-6,  
674-38-4, 91609-06-2; (finasteride) 98319-26-7; (doxazosin)  
74191-85-8; (tamsulosin) 80223-99-0; (terazosin)  
63074-08-8, 63590-64-7; (oxybutynin) 1508-65-2, 5633-20-5;  
(propantheline bromide) 298-50-0, 50-34-0;  
(phenylpropanolamine) 14838-15-4, 154-41-6, 4345-16-8,  
48115-38-4; (pseudoephedrine) 345-78-8, 7460-12-0, 90-82-4;  
(desipramine) 50-47-5, 58-28-6; (doxepin) 1229-29-4,  
1668-19-5; (imipramine) 113-52-0, 50-49-7; (nortriptyline)  
72-69-5, 894-71-3; (theophylline) 58-55-9, 5967-84-0,  
8055-07-0, 8061-56-1, 99007-19-9

L141 ANSWER 24 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999208638 EMBASE

TITLE: Effects of a .beta.2-agonist on airway hyperreactivity in  
subjects with cervical spinal cord injury.

AUTHOR: DeLuca R.V.; Grimm D.R.; Lesser M.; Bauman W.A.; Almenoff P.L.  
CORPORATE SOURCE: Dr. M. Lesser, Spinal Cord Damage Research, 130 West Kingsbridge Road, Bronx, NY 10468, United States  
SOURCE: Chest, (1999) 115/6 (1533-1538).  
Refs: 41  
ISSN: 0012-3692 CODEN: CHETBF  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 008 Neurology and Neurosurgery  
015 Chest Diseases, Thoracic Surgery and Tuberculosis  
033 Orthopedic Surgery  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ABSTRACT: Study Objective: Aerosolized ipratropium bromide or orally administered baclofen or oxybutynin chloride (Ditropan) block methacholine-associated airway hyperreactivity in subjects with chronic cervical spinal cord injury (SCI), whereas these agents do not inhibit airway hyperreactivity associated with the inhalation of histamine. The present study was performed to determine whether pretreatment with a .beta.2-agonist attenuates airway hyperresponsiveness in these subjects. Participants: Subjects with chronic cervical SCI previously demonstrating airway hyperreactivity were challenged with methacholine (n = 9) or histamine (n = 16) alone and, on a separate day, 25 min following inhalation of nebulized metaproterenol sulfate. Results: Inhalation of the .beta.2-agonist was associated with an increase in provocative concentration causing a 20% decrease in FEV1 (PC20) values (geometric mean) from 1.01 +/- 2.76 to 20.54 +/- 6.24 mg/mL for methacholine and from 2.29 +/- 2.26 to 19.82 +/- 5.93 mg/mL for histamine. No correlation was found between specific PC20 values for individual subjects and percentage improvement in FEV1 (liter) following inhalation of metaproterenol sulfate and between PC20 values and baseline FEV1 percent. Conclusion: These data, combined with findings that patients with chronic high cervical SCI experience increased breathlessness following exposure to exogenous agents, suggest that long-term prophylactic .beta.2-agonist therapy may reduce respiratory symptoms associated with airway hyperreactivity in these patients.

CONTROLLED TERM: Medical Descriptors:  
\*bronchus hyperreactivity: DT, drug therapy  
\*bronchus hyperreactivity: PC, prevention  
\*cervical spinal cord injury: DT, drug therapy  
disease association  
drug effect  
aerosol  
provocation test  
forced expiratory volume  
dyspnea  
prophylaxis  
spirometry  
smoking  
quadriplegia: DT, drug therapy  
bronchospasm  
human  
male  
clinical article  
clinical trial  
aged  
adult  
oral drug administration  
inhalational drug administration  
article  
priority journal

## Drug Descriptors:

\*beta 2 adrenergic receptor stimulating agent: DT, drug therapy  
\*ipratropium bromide: CT, clinical trial  
\*ipratropium bromide: CM, drug comparison  
\*ipratropium bromide: DT, drug therapy  
\*oxybutynin: CT, clinical trial  
\*oxybutynin: CB, drug combination  
\*oxybutynin: CM, drug comparison  
\*oxybutynin: DT, drug therapy  
methacholine  
histamine  
orciprenaline  
diazepam: CB, drug combination  
diazepam: DT, drug therapy  
amitriptyline: CB, drug combination  
amitriptyline: DT, drug therapy  
docusate sodium: CB, drug combination  
docusate sodium: DT, drug therapy  
baclofen: CB, drug combination  
baclofen: DT, drug therapy  
prazosin: CB, drug combination  
prazosin: DT, drug therapy  
captopril: CB, drug combination  
captopril: DT, drug therapy  
butalbital: CB, drug combination  
butalbital: DT, drug therapy  
phenytoin: CB, drug combination  
phenytoin: DT, drug therapy  
methenamine mandelate: CB, drug combination  
methenamine mandelate: DT, drug therapy  
cimetidine: CB, drug combination  
CAS REGISTRY NO.: (ipratropium bromide) 22254-24-6; (oxybutynin) 1508-65-2,  
5633-20-5; (methacholine) 55-92-5; (histamine) 51-45-6,  
56-92-8, 93443-21-1; (orciprenaline) 586-06-1, 5874-97-5;  
(diazepam) 439-14-5; (amitriptyline) 50-48-6, 549-18-8;  
(docusate sodium) 577-11-7; (baclofen) 1134-47-0;  
(prazosin) 19216-56-9, 19237-84-4; (captopril) 62571-86-2;  
(butalbital) 51005-25-5, 77-26-9; (phenytoin) 57-41-0,  
630-93-3; (methenamine mandelate) 587-23-5; (cimetidine)  
51481-61-9, 70059-30-2

L141 ANSWER 25 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96373790 EMBASE

DOCUMENT NUMBER: 1996373790

TITLE: Clozapine-induced urinary incontinence: Incidence and treatment with ephedrine.

AUTHOR: Fuller M.A.; Borovicka M.C.; Jaskiw G.E.; Simon M.R.; Kwon K.; Konicki P.E.

CORPORATE SOURCE: Pharmacy Service 119(B), 10000 Brecksville Road, Brecksville, OH 44141, United States

SOURCE: Journal of Clinical Psychiatry, (1996) 57/11 (514-518). ISSN: 0160-6689 CODEN: JCLPDE

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 028 Urology and Nephrology  
032 Psychiatry  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

## ABSTRACT:

Background: Treatment with the atypical antipsychotic drug clozapine appears to

be associated with an increased incidence of urinary incontinence (UI). We posited that the potent anti-.alpha.-adrenergic effects of clozapine were involved, and hence that an .alpha.-adrenergic agonist would reduce UI. We tested this hypothesis by using ephedrine, an approved .alpha.-adrenergic agonist. Method: Fifty-seven inpatients with schizophrenia or schizoaffective disorder (DSM-IV) who met the Kane criteria for being treatment refractory were treated with clozapine (75-900 mg/day). Patients who developed UI were then openly treated with ephedrine in increasing doses until UI was attenuated or a dose of 150 mg/day was attained. Results: Seventeen patients developed UI as evidenced by either urine-stained sheets/clothing or direct patient reports. In 2 cases, the UI was sufficiently severe that adult diapers had to be used. Comparison of patients who developed UI and those who did not showed that UI was associated with female gender and with concomitant treatment with typical antipsychotic drugs. One patient was treated with a behavioral program, but the remaining 16 patients were treated with ephedrine. Ephedrine treatment was very effective, with 15/16 patients showing improvement within 24 hours after reaching maximum ephedrine dosage. Twelve of 16 (including the 2 most severe) eventually had a complete remission of their UI. In the remaining 4 patients, 3 had a reduction in the frequency of UI and 1 showed no response. These benefits have been maintained over the course of 12 months of subsequent treatment for several patients. There were no side effects associated with the use of ephedrine nor were there any changes in neuropsychiatric status. Conclusion: Ephedrine appears to be a safe and effective treatment for clozapine-associated UI. By inference, it is likely that clozapine may cause UI via its anti-.alpha.-adrenergic properties.

CONTROLLED TERM: Medical Descriptors:  
\*urine incontinence: DT, drug therapy  
\*urine incontinence: SI, side effect  
adult  
aged  
article  
clinical trial  
drug efficacy  
female  
human  
major clinical study  
male  
oral drug administration  
priority journal  
risk factor  
schizoidism: DT, drug therapy  
schizoidism: DR, drug resistance  
schizophrenia: DT, drug therapy  
schizophrenia: DR, drug resistance  
Drug Descriptors:  
\*alpha adrenergic receptor stimulating agent: CT, clinical trial  
\*alpha adrenergic receptor stimulating agent: DT, drug therapy  
\*clozapine: DT, drug therapy  
\*clozapine: CB, drug combination  
\*clozapine: AE, adverse drug reaction  
\*ephedrine: DT, drug therapy  
\*ephedrine: CT, clinical trial  
\*neuroleptic agent: DT, drug therapy  
\*neuroleptic agent: AE, adverse drug reaction  
amantadine: CB, drug combination  
amantadine: DT, drug therapy  
benzatropine: DT, drug therapy  
benzatropine: CB, drug combination  
benzatropine mesilate  
benzodiazepine derivative: DT, drug therapy

benzodiazepine derivative: CB, drug combination  
beta adrenergic receptor blocking agent: CB, drug combination  
beta adrenergic receptor blocking agent: DT, drug therapy  
cholinergic receptor blocking agent: CB, drug combination  
cholinergic receptor blocking agent: DT, drug therapy  
doxazosin: CB, drug combination  
doxazosin: DT, drug therapy  
haloperidol: DT, drug therapy  
oxybutynin: DT, drug therapy  
oxybutynin: CB, drug combination  
propranolol: CB, drug combination  
propranolol: DT, drug therapy  
trihexyphenidyl:

CAS REGISTRY NO.: (clozapine) 5786-21-0; (ephedrine) 299-42-3, 50-98-6;  
(amantadine) 665-66-7, 768-94-5; (benzatropine) 86-13-5;  
(benzatropine mesilate) 132-17-2; (doxazosin) 74191-85-8;  
(haloperidol) 52-86-8; (oxybutynin) 1508-65-2, 5633-20-5;  
(propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1,  
525-66-6; (trihexyphenidyl) 144-11-6, 52-49-3  
CHEMICAL NAME: Clozaril; Cardura; Ditropan; Symmetrel; Cogentin; Haldol;  
Inderal; Artane

L141 ANSWER 26 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 97019409 EMBASE

DOCUMENT NUMBER: 1997019409

TITLE: McN-A-343 increases renal sympathetic nerve activity and  
blood pressure by a muscarinic and a non-muscarinic  
mechanism in the rat.

AUTHOR: Martin J.R.

CORPORATE SOURCE: J.R. Martin, Department of Pharmacology, Kirksville  
Coll.Osteopathic Medicine, Kirksville, MO 63501, United  
States

SOURCE: Journal of Autonomic Pharmacology, (1996) 16/5 (281-292).  
Refs: 36

ISSN: 0144-1795 CODEN: JAPHDU

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 002 Physiology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

1. Intravenous administration of the putative M1 muscarinic agonist McN-A-343 to conscious rats evokes an increase in mean arterial pressure (MAP) which can be blocked by muscarinic receptor antagonists. The present study was undertaken to evaluate the increase in MAP and renal sympathetic nerve activity (RSNA) evoked by intravenous administration of McN-A-343 to urethane-anaesthetized rats. 2. McN-A-343 (0.1-0.3 mg kg<sup>-1</sup>) evoked a concurrent increase in MAP and RSNA which could be inhibited by the nonselective muscarinic receptor antagonist methylatropine or the selective M1 muscarinic receptor antagonist telenzepine. Administration of higher doses of McN-A-343 (0.3-1.2 mg kg<sup>-1</sup>) in the presence of muscarinic receptor blockade evoked brief bursts in RSNA accompanied by increases in MAP. 3. The increases in MAP, but not the increases in RSNA, evoked by all doses of McN-A-343 could be attenuated by the selective .alpha.1-adrenoceptor antagonist prazosin. Adding the selective .alpha.2-adrenoceptor antagonist yohimbine to prazosin did not further inhibit the presser response to the low doses of McN-A-343. 4. The irreversible .alpha.-adrenoceptor and NPY receptor antagonist benextramine also attenuated the presser response evoked by the low doses of McN-A-343 but not the increases in RSNA. However, when combined with muscarinic receptor blockade, benextramine

completely inhibited the brief bursts in RSNA, and thus also the increases in MAP, evoked by the high doses of McN-A-343. 5. The pressor response remaining after the administration of high doses of McN-A-343 to rats pretreated with prazosin and methylatropine was inhibited by treatment with .alpha.,.beta.-methylene ATP. 6. These results show that McN-A-343 evokes increases in RSNA by muscarinic and non-muscarinic mechanisms. Furthermore, the subsequent increase in MAP is primarily dependent upon activation of vascular .alpha.1-adrenoceptors, but may also involve activation of P(2x) receptors.

## CONTROLLED TERM:

## Medical Descriptors:

- \*blood pressure
- \*kidney nerve
- animal experiment
- article
- controlled study
- intravenous drug administration
- male
- nonhuman
- rat

## Drug Descriptors:

- \*[4 [(3 chlorophenyl)carbamoyloxy] 2 butynyl]trimethylammonium: PD, pharmacology
- \*[4 [(3 chlorophenyl)carbamoyloxy] 2 butynyl]trimethylammonium: DO, drug dose
- benextramine: CB, drug combination
- benextramine: PD, pharmacology
- benextramine: CM, drug comparison
- methylatropine: PD, pharmacology
- methylatropine: CB, drug combination
- methylatropine: CM, drug comparison
- muscarinic agent: PD, pharmacology
- muscarinic agent: CM, drug comparison
- muscarinic agent: CB, drug combination
- muscarinic receptor blocking agent: CB, drug combination**
- muscarinic receptor blocking agent: CM, drug comparison
- muscarinic receptor blocking agent: PD, pharmacology
- neuropeptide y receptor antagonist: PD, pharmacology
- neuropeptide y receptor antagonist: CM, drug comparison
- neuropeptide y receptor antagonist: CB, drug combination

**prazosin: CB, drug combination**

- prazosin: CM, drug comparison
- prazosin: PD, pharmacology
- telenzepine: CM, drug comparison
- telenzepine: PD, pharmacology
- telenzepine: CB, drug combination
- yohimbine: CB, drug combination
- yohimbine: CM, drug comparison
- yohimbine: PD, pharmacology

## CAS REGISTRY NO.:

- (([4 [(3 chlorophenyl)carbamoyloxy] 2 butynyl]trimethylammonium) 55-45-8; (benextramine) 68535-69-3; (methylatropine) 31610-87-4; (prazosin) 19216-56-9, 19237-84-4; (telenzepine) 80880-90-6; (yohimbine) 146-48-5, 65-19-0

## CHEMICAL NAME:

- (1) Mcn a 343

## COMPANY NAME:

- (1) Rbi; Sigma

L141 ANSWER 27 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 96081858 EMBASE

DOCUMENT NUMBER: 1996081858

TITLE: Effect of receptor blockers on brain natriuretic peptide and C-type natriuretic peptide caused anxiolytic state in rats.

AUTHOR: Biro E.; Toth G.; Telegdy G.  
CORPORATE SOURCE: Department Pathophysiology, Albert Szent-Gyorgyi Medical  
Univ., P.O. Box 531, 6701 Szeged, Hungary  
SOURCE: Neuropeptides, (1996) 30/1 (59-65).  
ISSN: 0143-4179 CODEN: NRPPDD  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 003 Endocrinology  
032 Psychiatry  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: English  
SUMMARY LANGUAGE: English

## ABSTRACT:

Effect of different doses of centrally administered brain natriuretic peptide (BNP) and C-type natriuretic peptide (CNP) were examined in rats with respect to anxiolytic properties in an elevated plus-maze model. BNP in doses of 100, 200 and 400 ng, and CNP in doses of 100 and 200 ng abolished the normal preference for the closed arms of the maze, and increased the percentage time spent in the open arms; this is consistent with an 'anxiolytic-like' effect. Doses of 50 and 1000 ng BNP, and of 25, 50, 400 and 1000 ng CNP produced no behavioural effects in the elevated plus-maze model. Pretreatment with an .alpha.-adrenoreceptor antagonist or a muscarinergic cholinergic blocker, antagonized the effect of 200 ng BNP in the elevated plus-maze test. The 'anxiolytic-like' effects of a BNP were not modulated by a dopaminergic blocker, an .alpha.-adrenoreceptor antagonist, a GABA receptor antagonist, a 5-HT receptor antagonist or an opiate antagonist. The 'anxiolytic-like' effect of CNP was prevented by a dopamine receptor antagonist, or an .alpha.- or .beta.-adrenoreceptor blocker but not by a muscarinergic cholinergic blocker, a GABA receptor, a 5-HT receptor antagonist or an opiate receptor antagonist. These results suggest that multiple neurotransmitter system activation might be responsible for the BNP and CNP-induced 'anxiolytic-like' activity.

## CONTROLLED TERM: Medical Descriptors:

\*anxiety  
animal experiment  
article  
behavior  
controlled study  
intracerebroventricular drug administration  
intraperitoneal drug administration  
male  
maze test  
nonhuman  
priority journal  
rat  
drug therapy  
Drug Descriptors:

\*alpha adrenergic receptor blocking agent: CB, drug combination  
\*alpha adrenergic receptor blocking agent: PD, pharmacology  
\*alpha adrenergic receptor blocking agent: IT, drug interaction  
\*anxiolytic agent: DV, drug development  
\*brain natriuretic peptide: PD, pharmacology  
\*brain natriuretic peptide: DO, drug dose  
\*brain natriuretic peptide: CB, drug combination  
\*brain natriuretic peptide: CM, drug comparison  
\*brain natriuretic peptide: IT, drug interaction  
\*dopamine receptor blocking agent: CM, drug comparison  
\*dopamine receptor blocking agent: CB, drug combination  
\*dopamine receptor blocking agent: PD, pharmacology  
4 aminobutyric acid receptor blocking agent: CM, drug

comparison  
4 aminobutyric acid receptor blocking agent: CB, drug combination  
4 aminobutyric acid receptor blocking agent: PD, pharmacology  
atropine: CM, drug comparison  
atropine: CB, drug combination  
atropine: IT, drug interaction  
atropine: PD, pharmacology  
bicuculline: CB, drug combination  
bicuculline: PD, pharmacology  
bicuculline: CM, drug comparison  
haloperidol: CB, drug combination  
haloperidol: PD, pharmacology  
haloperidol: CM, drug comparison  
methysergide: PD, pharmacology  
methysergide: CM, drug comparison  
methysergide: CB, drug combination  
muscarinic receptor blocking agent: PD, pharmacology  
muscarinic receptor blocking agent: IT, drug interaction  
**muscarinic receptor blocking agent: CB, drug combination**  
muscarinic receptor blocking agent: CM, drug comparison  
naloxone: CB, drug combination  
naloxone: CM, drug comparison  
naloxone: PD, pharmacology  
natriuretic peptide: PD, pharmacology  
natriuretic peptide: CB, drug combination  
natriuretic peptide: CM, drug comparison  
natriuretic peptide: IT, drug interaction  
natriuretic peptide: DO, drug dose  
opiate antagonist: PD, pharmacology  
opiate antagonist: CM, drug comparison  
opiate antagonist: CB, drug combination  
phenoxybenzamine: CM, drug comparison  
phenoxybenzamine: CB, drug combination  
phenoxybenzamine: PD, pharmacology  
phenoxybenzamine: IT, drug interaction  
propranolol: CB, drug combination  
propranolol: IT, drug interaction  
propranolol: PD, pharmacology  
serotonin antagonist: CM, drug comparison  
serotonin antagonist: CB, drug combination  
serotonin antagonist: PD, pharmacology  
unclassified drug  
CAS REGISTRY NO.: (brain natriuretic peptide) 114471-18-0; (atropine) 51-55-8, 55-48-1; (bicuculline) 485-49-4; (haloperidol) 52-86-8; (methysergide) 16509-15-2, 361-37-5, 62288-72-6; (naloxone) 357-08-4, 465-65-6; (phenoxybenzamine) 59-96-1, 63-92-3; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6  
COMPANY NAME: Bachem (United States); Smith kline and french (United Kingdom); Sigma (United States); Sandoz (Germany); Endo laboratories (United States); Egys (Hungary)  
L141 ANSWER 28 OF 31 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 92346906 EMBASE  
DOCUMENT NUMBER: 1992346906  
TITLE: Clinical pharmacology in neurourology.  
AUTHOR: Appell R.A.  
CORPORATE SOURCE: Department of Urology, Louisiana State Univ. Medical Center, 1542 Tulane Avenue, New Orleans, LA 70112-2822, United States

SOURCE: Problems in Urology, (1992) 6/4 I (622-642).  
ISSN: 0889-471X CODEN: PRUREX  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 028 Urology and Nephrology  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Pharmacotherapy may be used to treat individuals with various voiding dysfunctions, especially those of a neurogenic etiology. Based upon the neurophysiology of the lower urinary tract, it would be expected that certain pharmacologic agents facilitate bladder emptying while others facilitate bladder storage. The clinical application of currently available pharmacologic agents in the management of neurogenic vesicourethral dysfunction is reviewed with regard to efficacy and safety of specific medications.

CONTROLLED TERM: Medical Descriptors:

- \*urinary dysfunction: DT, drug therapy
- binding site
- bladder contraction
- bladder pressure
- drug contraindication
- drug mechanism
- drug potentiation
- human
- intravenous drug administration
- micturition
- oral drug administration
- review

Drug Descriptors:

- \*alpha adrenergic receptor blocking agent: PD, pharmacology
- \*alpha adrenergic receptor blocking agent: DT, drug therapy
- \*muscarinic receptor blocking agent: PD, pharmacology
- \*muscarinic receptor blocking agent: DT, drug therapy
- \*muscle relaxant agent: PD, pharmacology
- \*muscle relaxant agent: DT, drug therapy
- \*spasmolytic agent: PD, pharmacology
- \*spasmolytic agent: DT, drug therapy
- \*tricyclic antidepressant agent: DT, drug therapy
- \*tricyclic antidepressant agent: PD, pharmacology
- alpha adrenergic receptor stimulating agent: DT, drug therapy
- baclofen: DT, drug therapy
- baclofen: PD, pharmacology
- benzodiazepine derivative: DT, drug therapy
- benzodiazepine derivative: PD, pharmacology
- beta adrenergic receptor blocking agent
- bethanechol: CB, drug combination
- bethanechol: DT, drug therapy
- bethanechol: PD, pharmacology
- chlorpromazine: DT, drug therapy
- dantrolene: PD, pharmacology
- dantrolene: DT, drug therapy
- dicycloverine: DT, drug therapy
- dicycloverine: PD, pharmacology
- estrogen: DT, drug therapy
- estrogen: PD, pharmacology
- flavoxate: DT, drug therapy
- flavoxate: PD, pharmacology
- haloperidol: DT, drug therapy
- imipramine: PD, pharmacology

L141 ANSWER 29 OF 31 WPIDS (C) 2003 THOMSON DERWENT  
 ACCESSION NUMBER: 2003-371870 [35] WPIDS  
 DOC. NO. CPI: C2003-098712  
 TITLE: Pharmaceutical composition useful for treating urinary disorders, comprising **combination** of muscarinic receptor or **alpha-adrenergic** receptor **antagonist**, 5 alpha reductase inhibitor and 5HT-1 alpha receptor agonist or antagonist.  
 DERWENT CLASS: B05  
 INVENTOR(S): ANDERSSON, P; ARNERIC, S P  
 PATENT ASSIGNEE(S): (ANDE-I) ANDERSSON P; (ARNE-I) ARNERIC S P; (PHAA) PHARMACIA AB  
 COUNTRY COUNT: 100  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC																
WO 2003026564	A2	20030403	(200335)*	EN	12	A61K000-00																	
RW:	AT	BE	BG	CH	CY	CZ	DE	DK	EA	EE	ES	FI	FR	GB	GH	GM	GR	IE	IT	KE	LS	LU	
	MC	MW	MZ	NL	OA	PT	SD	SE	SK	SL	SZ	TR	TZ	UG	ZM	ZW							
W:	AE	AG	AL	AM	AT	AU	AZ	BA	BB	BG	BR	BY	BZ	CA	CH	CN	CO	CR	CU	CZ	DE	DK	
	DM	DZ	EC	EE	ES	FI	GB	GD	GE	GH	GM	HR	HU	ID	IL	IN	IS	JP	KE	KG	KP	KR	
	KZ	LC	LK	LR	LS	LT	LU	LV	MA	MD	MG	MK	MN	MW	MX	MZ	NO	NZ	OM	PH	PL	PT	
	RO	RU	SD	SE	SG	SI	SK	SL	TJ	TM	TN	TR	TT	TZ	UA	UG	US	UZ	VN	YU	ZA	ZM	
	ZW																						
US 2003060513	A1	20030327	(200335)			A61K031-137																	

PATENT NO	KIND	APPLICATION	DATE
WO 2003026564	A2	WO 2002-SE1748	20020926
US 2003060513	A1	US 2001-965556	20010927

Searched by Barb O'Bryen, STIC 308-4291

20010927

## INT. PATENT CLASSIF.:

MAIN: A61K000-00; A61K031-137

## BASIC ABSTRACT:

WO2003026564 A UPAB: 20030603

NOVELTY - A pharmaceutical composition (A) comprises:

(i) compound (I) selected from **muscarinic** receptor**antagonist**, 5 alpha -reductase inhibitor and **alpha -****adrenergic** receptor **antagonists** or its precursors andsalts (preferably **muscarinic** receptor **antagonist**);

(ii) compound (II) selected from 5-HT-1 alpha receptor agonist or antagonist or its salts (preferably 5-HT-1 alpha receptor antagonist); and

(iii) optionally carrier or diluent.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for therapeutic treatment of urinary disorder in a mammal including humans comprising (I), (II) and optionally instructions for use.

ACTIVITY - Uropathic; Antidepressant; Tranquilizer.

MECHANISM OF ACTION - Unstable bladder contraction inhibitor.

USE - For treating urinary disorders such as lower urinary tract symptoms, unstable or overactive urinary bladder, bladder outflow obstructions, urinary incontinence, stress incontinence, interstitial cystitis and associated depression in mammals including humans (all claimed).

ADVANTAGE - The composition provides rapid relief from urinary disorders by inhibiting or suppressing unstable bladder contractions and diminishing problems associated with incomplete bladder emptying, with minimal amount of deleterious side effects and hence improving the quality of life.

Dwg.0/0

FILE SEGMENT:

CPI

FIELD AVAILABILITY:

AB; DCN

MANUAL CODES:

CPI: B06-A01; B10-B02G; B10-B03B; B14-D05D; B14-J01A1;  
B14-J02B2; B14-J02D1; B14-J03; B14-J04; B14-L01;  
B14-N07

L141 ANSWER 30 OF 31

WPIDS (C) 2003 THOMSON DERWENT

ACCESSION NUMBER:

2003-229267 [22] WPIDS

DOC. NO. CPI:

C2003-058832

TITLE:

Drug delivery device for controlled release of an active agent comprises a composition having a core and a coating having pore-forming element having dissolution rate slower than the release rate the active ingredients..

DERWENT CLASS:

A96 B05 B07 C03 C07 D22

INVENTOR(S):

CHOPRA, S; CHOPRA, S K

PATENT ASSIGNEE(S):

(CHOP-I) CHOPRA S; (CHOP-I) CHOPRA S K; (SAVI-N) SAVIT CONSULTING INC

COUNTRY COUNT:

100

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG MAIN IPC

WO 2002094227 A1 20021128 (200322)\* EN 26 A61K009-22

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
NL OA PT SD SE SL SZ TR TZ UG ZM ZWW: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK  
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR  
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT  
RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

US 2003003151 A1 20030102 (200322) A61K009-24

APPLICATION DETAILS:

PATENT NO KIND

APPLICATION

DATE

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WO 2002094227 A1                      WO 2002-IB1854      20020524  
US 2003003151 A1 Provisional        US 2001-293701P    20010525  
                                         US 2002-85234      20020228

PRIORITY APPLN. INFO: US 2002-85234      20020228; US 2001-293701P  
                                         20010525

INT. PATENT CLASSIF.:

MAIN:            A61K009-22; A61K009-24

SECONDARY:      A61K009-28; A61K009-30; A61K009-32; A61K009-36

BASIC ABSTRACT:

WO 200294227 A UPAB: 20030402

NOVELTY - A dissolution and diffusion device comprises a shaped core having planar release face and a compressed **mixture** of an active ingredient. The compressed core is coated, except for at least one exposed face. The pore-forming elements have a dissolution rate slower than the release rate so that the pore formation is completed after release of the active ingredients and the residual inert structures disintegrate.

DETAILED DESCRIPTION - A dissolution and diffusion device comprises a shaped core (a) and a coating (b). (a) comprises at least one planar release face in which the dimensions of the face remain constant throughout a substantial portion of the delivery period, a compressed **mixture** of active ingredient homogenously mixed with at least one dissolution regulator operable to release the active ingredient from the release face and optionally a score circumscribed on the surface to secure the coating. (b) surrounds and adheres to the core except the release faces. The coating contains an insoluble polymer and pore-forming elements operable to create channels in the insoluble coating to permit disintegration of the coating after release of the active ingredient is completed.

INDEPENDENT CLAIMS are included for the following:

(1) Preparation of a chemical delivery device by dry granulation involving (a1) blending the active ingredient and a dissolution regulator and optionally with a diluent, (b1) optionally milling and sieving the resulting blend with a mesh size suitable for the specific application, (c1) mixing the blend with a soluble or insoluble lubricant and compressing the blend into tablet in punch machine, and (d1) coating the tablet with a **mixture** of an insoluble polymer and pore-forming elements using a compression-coating machine;

(2) Preparation of a chemical delivery device by wet granulation involving blending the active ingredient and a dissolution regulator with water and/or an organic solvent and optionally with a diluent, drying the resulting blend, and steps (b1), (c1) and (d1);

(3) Delivering a constant controlled release of an active compound into a fluid medium involving incorporating at least one biologically active ingredient into a tablet comprising (a) and (b) and placing the tablet in a fluid medium; and

(4) Dissolution controlled chemical device providing controlled variable release of at least one biological active ingredient into a fluid medium through out a portion of the delivery period involving (a) and (b).

USE - For controlled release of an active agent for human or veterinary use (claimed).

ADVANTAGE - The device can deliver an active ingredient at a constant or controlled variable rate. The device can readily be scaled to different proportions to accommodate differing quantities of the active chemical, and thus have the capacity for longer release periods. As the core is slow dissolving, dose dumping is not prevalent in the delivery device. The hydrodynamic conditions prevailing in the stomach are minimized as only the peripheral face of the core is exposed. The device is reliable, predictable and insures disintegration of the insoluble impermeable coating to avoid elimination of the intact device. The rate of disintegration of the coating can be manipulated by adjusting the size,

density and composition of the pore-forming materials.

Dwg.0/6

FILE SEGMENT: CPI  
FIELD AVAILABILITY: AB; DCN  
MANUAL CODES: CPI: A12-V01; B04-C02A; B04-C03; B11-C03; B11-C04;  
B12-M10; B12-M11B; C04-C02A; C04-C03; C11-C03;  
C11-C04; C12-M10; C12-M11B; D09-C01

L141 ANSWER 31 OF 31 WPIDS (C) 2003 THOMSON DERWENT  
ACCESSION NUMBER: 2002-666878 [71] WPIDS  
DOC. NO. CPI: C2002-187190  
TITLE: Preparation of deformable syntactic foams useful as  
pharmaceutical carriers for the delivery of a compound or  
a chemical involves mixing a resin, binder and a  
stabilizer and reacting the **mixture** with an  
organic solvent.  
DERWENT CLASS: A96 B05 B07  
INVENTOR(S): ODIDI, A; ODIDI, I  
PATENT ASSIGNEE(S): (ODID-I) ODIDI A; (ODID-I) ODIDI I  
COUNTRY COUNT: 100  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2002056861	A2	20020725	(200271)*	EN	47	A61K009-00	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW							

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002056861	A2	WO 2002-CA54	20020117

PRIORITY APPLN. INFO: US 2001-765783 20010119

INT. PATENT CLASSIF.:

MAIN: A61K009-00

BASIC ABSTRACT:

WO 200256861 A UPAB: 20021105  
NOVELTY - Preparation of a deformable syntactic foam comprises (a) mixing together at least one homopolymer resin, at least one binder and at least one stabilizer to form a blended **mixture** having a LOD of 1 - 10%, and (b) reacting the blended **mixture** with at least one organic solvent under high shear conditions at 10 - 25 deg. C until a foam composition deformable to touch is formed.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

- (1) Manufacturing a pharmaceutical carrier comprising:
  - (a) mixing together at least one homopolymer resin, binder, microspheres and stabilizer to form a blended **mixture** having a LOD of 1 - 10%,
  - (b) reacting the blended **mixture** with at least one organic solvent under high shear conditions at 10 - 25 deg. C until a foam composition deformable to touch is formed;
  - (c) reducing the size of the deformable syntactic foam to reassemble into a shaped composite;
- (2) A pharmaceutical composition comprising a pharmaceutical and a

pharmaceutical carrier; and

(3) A syntactic foam of elongate threads comprising homopolymer resin, binder, microsphere and a stabilizer.

USE - As a pharmaceutical carrier for the delivery of a compound or a chemical (claimed) including pharmaceuticals. Also useful as carriers, coated or uncoated for chemicals, biological agents, nutraceuticals, growth factors, amino acids, bioactive materials and pharmaceutically active and inactive materials and have pharmaceutical, sanitary, veterinary, agricultural and medical applications.

ADVANTAGE - The foam is deformable and compressible. The foam permits the time release of pharmaceuticals in mammals particularly humans and reduces the frequency of taking a particular medicine. The foam is safe, stable and can be prepared by economical and versatile manufacturing processes.

Dwg.0/9

FILE SEGMENT:

FIELD AVAILABILITY:

MANUAL CODES:

CPI

AB; DCN

CPI: A12-V01; A12-W12; B01-A02; B01-D02; B02-A; B02-C03;  
B02-E; B04-C02A1; B04-C03B; B04-C03D; B05-A01B;  
B05-B01G; B05-B02C; B06-F03; B06-H; B07-A02B; B07-H;  
B08-D01; B10-A07; B10-A08; B10-A12C; B10-A13D;  
B10-A18; B10-A19; B10-B02F; B10-B03B; B10-B04;  
B10-C03; B10-C04B; B11-C01C

=> fil capl; d que 134

FILE 'CAPLUS' ENTERED AT 11:58:47 ON 04 JUN 2003

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FILE COVERS 1907 - 4 Jun 2003 VOL 138 ISS 23

FILE LAST UPDATED: 3 Jun 2003 (20030603/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

L4	1	SEA FILE=REGISTRY ABB=ON	210538-44-6
L5	3	SEA FILE=REGISTRY ABB=ON	DOXAZOSIN?/CN
L6	3	SEA FILE=REGISTRY ABB=ON	TERAZOSIN?/CN
L7	1	SEA FILE=REGISTRY ABB=ON	ABANOQUIL/CN
L8	5	SEA FILE=REGISTRY ABB=ON	PRAZOSIN?/CN
L9	5	SEA FILE=REGISTRY ABB=ON	INDORAMIN?/CN
L10	2	SEA FILE=REGISTRY ABB=ON	DARIFENACIN?/CN
L11	2	SEA FILE=REGISTRY ABB=ON	TOLTERODINE?/CN
L12	3	SEA FILE=REGISTRY ABB=ON	OXYBUTYNIN?/CN
L13	2860	SEA FILE=CAPLUS ABB=ON	ADRENOCEPTOR ANTAGONISTS+OLD/CT(L) ALPHA
L14	1702	SEA FILE=CAPLUS ABB=ON	ALPHA(L) (ADRENOCEPTOR ANTAGONIST#)/OBI
L15	2879	SEA FILE=CAPLUS ABB=ON	(L4 OR L5 OR L6 OR L7 OR L8 OR L9)
L16	2566	SEA FILE=CAPLUS ABB=ON	(DOXAZOSIN# OR TETRAZOSIN# OR TERAZOSIN# OR ABANOQUIL# OR PRAZOSIN# OR INDORAMIN#)/OBI
L17	1465	SEA FILE=CAPLUS ABB=ON	MUSCARINIC ANTAGONISTS+OLD/CT
L18	1859	SEA FILE=CAPLUS ABB=ON	MUSCARINIC (2A) ANTAGONIST#/OBI
L19	472	SEA FILE=CAPLUS ABB=ON	(L10 OR L11 OR L12)
L20	479	SEA FILE=CAPLUS ABB=ON	(DARIFENACIN# OR TOLTERODIN# OR OXYBUTYNIN#)/OBI
L25	3732	SEA FILE=CAPLUS ABB=ON	URINARY TRACT/CT
L26	23839	SEA FILE=CAPLUS ABB=ON	PROSTATE GLAND/CT
L27	2616	SEA FILE=CAPLUS ABB=ON	BENIGN(A) HYPERPLAS?
L28	15375	SEA FILE=CAPLUS ABB=ON	BLADDER/CT
L29	1019	SEA FILE=CAPLUS ABB=ON	URETHRA/CT
L34	16	SEA FILE=CAPLUS ABB=ON	(L13 OR L14 OR L15 OR L16) AND (L17 OR L18 OR L19 OR L20) AND (L25 OR L26 OR L27 OR L28 OR L29)

=> s 134 not 133

L142 13 L34 NOT L33 *previously printed*

=> fil medl; d que 161; d que 162

FILE 'MEDLINE' ENTERED AT 11:58:49 ON 04 JUN 2003

FILE LAST UPDATED: 3 JUN 2003 (20030603/UP). FILE COVERS 1958 TO DATE.

On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See <http://www.nlm.nih.gov/mesh/changes2003.html> for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L4 1 SEA FILE=REGISTRY ABB=ON 210538-44-6  
L5 3 SEA FILE=REGISTRY ABB=ON DOXAZOSIN?/CN  
L6 3 SEA FILE=REGISTRY ABB=ON TERAZOSIN?/CN  
L7 1 SEA FILE=REGISTRY ABB=ON ABANOQUIL/CN  
L8 5 SEA FILE=REGISTRY ABB=ON PRAZOSIN?/CN  
L9 5 SEA FILE=REGISTRY ABB=ON INDORAMIN?/CN  
L10 2 SEA FILE=REGISTRY ABB=ON DARIFENACIN?/CN  
L11 2 SEA FILE=REGISTRY ABB=ON TOLTERODINE?/CN  
L12 3 SEA FILE=REGISTRY ABB=ON OXYBUTYNIN?/CN  
L35 885 SEA FILE=MEDLINE ABB=ON RECEPTORS, ADRENERGIC, ALPHA+NT/CT(L)A  
I/CT  
L36 6827 SEA FILE=MEDLINE ABB=ON (L4 OR L5 OR L6 OR L7 OR L8 OR L9)  
L37 6643 SEA FILE=MEDLINE ABB=ON DOXAZOSIN/CT OR PRAZOSIN/CT  
L38 529 SEA FILE=MEDLINE ABB=ON TETRAZOSIN# OR TERAZOSIN# OR HYTRIN#  
OR A45975 OR A 45975 OR ABANOQUIL OR UK52046 OR UK 52046  
L39 283 SEA FILE=MEDLINE ABB=ON INDORAMIN# OR WY21901 OR WY 21901  
L40 475 SEA FILE=MEDLINE ABB=ON (L10 OR L11 OR L12)  
L41 652 SEA FILE=MEDLINE ABB=ON DARIFEN!CIN# OR TOLTERODIN# OR DETROL  
OR OXYBUTYNIN# OR CYSTRIN# OR OXYTROL#  
L42 191414 SEA FILE=MEDLINE ABB=ON DRUG INTERACTIONS+NT/CT OR DRUG  
COMBINATIONS+NT/CT OR DRUG THERAPY, COMBINATION/CT  
L44 15978 SEA FILE=MEDLINE ABB=ON PROSTATE/CT  
L45 11277 SEA FILE=MEDLINE ABB=ON PROSTATIC HYPERPLASIA/CT  
L46 37197 SEA FILE=MEDLINE ABB=ON ADRENERGIC ALPHA-ANTAGONISTS+NT/CT  
L47 40225 SEA FILE=MEDLINE ABB=ON MUSCARINIC ANTAGONISTS+NT/CT  
L48 966 SEA FILE=MEDLINE ABB=ON ((L35 OR L36 OR L37 OR L38 OR L39) OR  
L46) AND (L47 OR (L40 OR L41)) AND L42  
L50 37304 SEA FILE=MEDLINE ABB=ON BLADDER/CT OR URETHRA/CT  
L60 5500 SEA FILE=MEDLINE ABB=ON URINATION/CT  
L61 6 SEA FILE=MEDLINE ABB=ON L48 AND (L50 OR L44 OR L45 OR L60)

L4 1 SEA FILE=REGISTRY ABB=ON 210538-44-6  
L5 3 SEA FILE=REGISTRY ABB=ON DOXAZOSIN?/CN  
L6 3 SEA FILE=REGISTRY ABB=ON TERAZOSIN?/CN  
L7 1 SEA FILE=REGISTRY ABB=ON ABANOQUIL/CN  
L8 5 SEA FILE=REGISTRY ABB=ON PRAZOSIN?/CN  
L9 5 SEA FILE=REGISTRY ABB=ON INDORAMIN?/CN  
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L11 2 SEA FILE=REGISTRY ABB=ON TOLTERODINE?/CN  
L12 3 SEA FILE=REGISTRY ABB=ON OXYBUTYNIN?/CN  
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I/CT  
L36 6827 SEA FILE=MEDLINE ABB=ON (L4 OR L5 OR L6 OR L7 OR L8 OR L9)  
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L38 529 SEA FILE=MEDLINE ABB=ON TETRAZOSIN# OR TERAZOSIN# OR HYTRIN#  
OR A45975 OR A 45975 OR ABANOQUIL OR UK52046 OR UK 52046  
L39 283 SEA FILE=MEDLINE ABB=ON INDORAMIN# OR WY21901 OR WY 21901  
L40 475 SEA FILE=MEDLINE ABB=ON (L10 OR L11 OR L12)

L41 652 SEA FILE=MEDLINE ABB=ON DARIFEN!CIN# OR TOLTERODIN# OR DETROL  
OR OXYBUTYNIN# OR CYSTRIN# OR OXYTROL#  
L45 11277 SEA FILE=MEDLINE ABB=ON PROSTATIC HYPERPLASIA/CT  
L50 37304 SEA FILE=MEDLINE ABB=ON BLADDER/CT OR URETHRA/CT  
L53 10288 SEA FILE=MEDLINE ABB=ON ADRENERGIC ALPHA-ANTAGONISTS/CT  
L54 3097 SEA FILE=MEDLINE ABB=ON MUSCARINIC ANTAGONISTS/CT  
L60 5500 SEA FILE=MEDLINE ABB=ON URINATION/CT  
L62 11 SEA FILE=MEDLINE ABB=ON ((L35 OR L36 OR L37 OR L38 OR L39) OR  
L53) AND (L54 OR L40 OR L41) AND (L50 OR L45 OR L60)

=> s (l61 or l62) not l139

L143 12 (L61 OR L62) NOT L139 *previously printed*

=> fil embase; d que l115; s l115 not l140

FILE 'EMBASE' ENTERED AT 11:58:50 ON 04 JUN 2003  
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FILE COVERS 1974 TO 29 May 2003 (20030529/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

L4 1 SEA FILE=REGISTRY ABB=ON 210538-44-6  
L5 3 SEA FILE=REGISTRY ABB=ON DOXAZOSIN?/CN  
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L7 1 SEA FILE=REGISTRY ABB=ON ABANOQUIL/CN  
L8 5 SEA FILE=REGISTRY ABB=ON PRAZOSIN?/CN  
L9 5 SEA FILE=REGISTRY ABB=ON INDORAMIN?/CN  
L10 2 SEA FILE=REGISTRY ABB=ON DARIFENACIN?/CN  
L11 2 SEA FILE=REGISTRY ABB=ON TOLTERODINE?/CN  
L12 3 SEA FILE=REGISTRY ABB=ON OXYBUTYNIN?/CN  
L86 5910 SEA FILE=EMBASE ABB=ON ALPHA ADRENERGIC RECEPTOR BLOCKING  
AGENT/CT  
L87 19321 SEA FILE=EMBASE ABB=ON (L4 OR L5 OR L6 OR L7 OR L8 OR L9)  
L88 2306 SEA FILE=EMBASE ABB=ON DOXAZOSIN/CT OR DOXAZOSIN DERIVATIVE/CT  
OR DOXAZOSIN MESYLATE/CT  
L89 1452 SEA FILE=EMBASE ABB=ON TERAZOSIN/CT  
L90 37 SEA FILE=EMBASE ABB=ON ABANOQUIL/CT  
L91 16803 SEA FILE=EMBASE ABB=ON PRAZOSIN/CT OR PRAZOSIN DERIVATIVE/CT  
L92 704 SEA FILE=EMBASE ABB=ON INDORAMIN/CT OR INDORAMIN DERIVATIVE/CT  
  
L93 2282 SEA FILE=EMBASE ABB=ON MUSCARINIC RECEPTOR BLOCKING AGENT/CT  
L94 1809 SEA FILE=EMBASE ABB=ON (L10 OR L11 OR L12)  
L95 92 SEA FILE=EMBASE ABB=ON DARIFENACIN/CT  
L96 410 SEA FILE=EMBASE ABB=ON TOLTERODINE/CT OR TOLTERODINE TARTRATE/  
CT  
L97 1627 SEA FILE=EMBASE ABB=ON OXYBUTYNIN/CT  
L98 230391 SEA FILE=EMBASE ABB=ON DRUG COMBINATION/CT  
L99 160218 SEA FILE=EMBASE ABB=ON DRUG INTERACTION+NT/CT  
L100 29617 SEA FILE=EMBASE ABB=ON BLADDER/CT OR URETHRA/CT  
L101 9575 SEA FILE=EMBASE ABB=ON PROSTATE HYPERTROPHY/CT  
L102 7252 SEA FILE=EMBASE ABB=ON MICTURITION/CT  
L103 1503 SEA FILE=EMBASE ABB=ON MICTURITION DISORDER/CT  
L115 14 SEA FILE=EMBASE ABB=ON (L86 OR L87 OR L88 OR L89 OR L90 OR  
L91 OR L92) AND (L93 OR L94 OR L95 OR L96 OR L97) AND (L100 OR  
L101 OR L102 OR L103) AND (L98 OR L99)

L144

11 L115 NOT L140

*previously printed*

=> fil wpids; d que 1135; s 1135 not 1137

FILE 'WPIDS' ENTERED AT 11:58:51 ON 04 JUN 2003  
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FILE LAST UPDATED: 3 JUN 2003 <20030603/UP>  
MOST RECENT DERWENT UPDATE: 200335 <200335/DW>  
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS <<<

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[http://www.derwent.com/userguides/dwpi\\_guide.html](http://www.derwent.com/userguides/dwpi_guide.html) <<<

L116 508 SEA FILE=WPIDS ABB=ON (ADRENOCEPTOR OR ADRENERGIC) (2A) ALPHA(2A)  
) (ANTAGONIST# OR BLOCK?)  
L117 112 SEA FILE=WPIDS ABB=ON DOXAZOSIN# OR CARDURA# OR UK33274 OR UK  
33274  
L118 79 SEA FILE=WPIDS ABB=ON TETRAZOSIN# OR TERAZOSIN# OR HYTRIN# OR  
A45975 OR A 45975  
L119 4 SEA FILE=WPIDS ABB=ON ABANOQUIL# OR UK52046 OR UK 52046  
L120 200 SEA FILE=WPIDS ABB=ON PRAZOSIN# OR FURAZOSIN# OR PRATSIOL#  
L121 31 SEA FILE=WPIDS ABB=ON INDORAMIN# OR WY21901 OR WY 21901  
L122 183 SEA FILE=WPIDS ABB=ON MUSCARINIC(2A) (ANTAGONIST# OR BLOCK?)  
L123 124 SEA FILE=WPIDS ABB=ON DARIFEN!CIN# OR TOLTERODIN# OR DETROL  
OR OXYBUTYNIN# OR CYSTRIN# OR OXYTROL#  
L124 12792 SEA FILE=WPIDS ABB=ON BLADDER# OR URETHRA?  
L126 7194 SEA FILE=WPIDS ABB=ON PROSTATE  
L127 5291 SEA FILE=WPIDS ABB=ON HYPERPLAS? OR HYPERTROPH?  
L134 9005 SEA FILE=WPIDS ABB=ON URINA?  
L135 5 SEA FILE=WPIDS ABB=ON (L116 OR L117 OR L118 OR L119 OR L120  
OR L121) AND (L122 OR L123) AND (L124 OR (L126 OR L127) OR  
L134)

L145

2 L135 NOT L137

*previously printed*

=> dup rem 1142,1143,1144,1145

FILE 'CAPLUS' ENTERED AT 11:59:15 ON 04 JUN 2003  
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PROCESSING COMPLETED FOR L142

PROCESSING COMPLETED FOR L143

PROCESSING COMPLETED FOR L144

PROCESSING COMPLETED FOR L145

L146 35 DUP REM L142 L143 L144 L145 (3 DUPLICATES REMOVED)

ANSWERS '1-13' FROM FILE CAPLUS

ANSWERS '14-25' FROM FILE MEDLINE

ANSWERS '26-35' FROM FILE EMBASE

=> d ibib ab hitrn 1-13; d iall 14-35; fil hom

L146 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1

ACCESSION NUMBER: 2002:122770 CAPLUS

DOCUMENT NUMBER: 136:178015

TITLE: Drugs for incontinence - salified and nonsalified  
nitric oxide-donors and phosphodiesterase inhibitors

INVENTOR(S): Del Soldato, Piero; Benedini, Francesca

PATENT ASSIGNEE(S): Nicox S.A., Fr.

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011707	A2	20020214	WO 2001-EP8734	20010727
WO 2002011707	A3	20021205		

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ,  
EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT,  
LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA,  
US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG.

AU 2001091691	A5	20020218	AU 2001-91691	20010727
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EP 1307184	A2	20030507	EP 2001-971798	20010727
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: IT 2000-MI1848 A 20000808  
WO 2001-EP8734 W 20010727

OTHER SOURCE(S): MARPAT 136:178015

AB Use in the incontinence of one or more of the following classes of drugs selected from the following: (B) salified and nonsalified nitric oxide-donor drugs, of formula: A - X1 - N(O)z, (B') nitrate salts of drugs used for the incontinence, and which do not contain in the mol. a nitric oxide donor group; (C) org. or inorg. salts of compds. inhibiting phosphodiesterases.

IT 1508-65-2, Oxybutynin hydrochloride

RL: PAC (Pharmacological activity); RCT (Reactant); THU (Therapeutic use);  
BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
(salified and nonsalified nitric oxide-donors and phosphodiesterase inhibitors for treatment of incontinence)

IT 5633-20-5 19216-56-9, Prazosin

74191-85-8, Doxazosin 124937-51-5,

Tolterodine 133099-04-4

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(salified and nonsalified nitric oxide-donors and phosphodiesterase

inhibitors for treatment of incontinence)

L146 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2  
ACCESSION NUMBER: 2001:228701 CAPLUS  
DOCUMENT NUMBER: 134:247264  
TITLE: Treatment of lower urinary tract symptoms with  
muscarinic and .alpha.-adrenergic antagonists and  
5.alpha.-reductase inhibitors, and pharmaceutical  
compositions for use therein  
INVENTOR(S): Stoner, Elizabeth; Drake, Paul J.; Bach, Mark A.  
PATENT ASSIGNEE(S): Merck & Co., Inc., USA  
SOURCE: PCT Int. Appl., 20 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021167	A1	20010329	WO 2000-US25534	20000918
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1999-155357P P 19990922  
OTHER SOURCE(S): MARPAT 134:247264

AB A medical condition in men known as Lower Urinary Tract Symptoms (LUTS) is treated by the administration of a muscarinic receptor antagonist in combination with at least one of a 5.alpha.-reductase inhibitor and an .alpha.-adrenergic receptor blocker.

IT 5633-20-5, Oxybutynin 19216-56-9,  
Prazosin 26844-12-2, Indoramin  
63590-64-7, Terazosin 74191-85-8,  
Doxazosin 90402-40-7, Abanoquil  
124937-51-5, Tolterodine 133099-04-4,  
Darifenacin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(muscarinic and .alpha.-adrenergic antagonists and 5.alpha.-reductase inhibitors for treatment of lower urinary tract symptoms , and pharmaceutical comps.)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L146 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2003:261600 CAPLUS  
DOCUMENT NUMBER: 138:276286  
TITLE: Pharmaceutical compositions contg. **muscarinic antagonists** and 5.alpha.-reductase inhibitors for urinary tract disorder treatment  
INVENTOR(S): Arneric, Stephen P.; Andersson, Per-Olof  
PATENT ASSIGNEE(S): Pharmacia AB, Swed.  
SOURCE: PCT Int. Appl., 23 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003026564	A2	20030403	WO 2002-SE1748	20020926

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003060513	A1	20030327	US 2001-965556	20010927
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PRIORITY APPLN. INFO.: US 2001-965556 A 20010927

SE 2001-3858 A 20011120

AB The present invention concerns the field of urol. The invention provides a pharmaceutical compn. comprising a combination of a first compd. selected from the group consisting of muscarinic receptor antagonists, 5.alpha.-reductase inhibitors, and .alpha.-adrenergic receptor antagonists, and precursors and salts, and a second compd. selected from the group consisting of 5-HT1a receptor agonists and antagonists, and precursors and salts thereof, and optionally a carrier or a diluent. There is also provided a method of treatment of urinary disorders in a mammal, including humans. A pharmaceutical compn. is prepd. by combining tolterodine with a neutral 5-HT1a receptor antagonist in a carrier. The compn. contains 0.05-4 mg tolterodine/kg patient body wt. (e.g., 3-240 mg tolterodine for a person weighing 60 kg) and 0.01-1 mg of neutral 5-HT1a receptor antagonist/kg of patient body wt. The compn. is administered to a patient for the treatment of incontinence, and particularly stress incontinence, urge incontinence or mixed incontinence.

IT 5633-20-5, Oxybutynin 124937-51-5,  
Tolterodine 124937-52-6 133099-04-4,

Darifenacin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical compns. contg. **muscarinic antagonists**

and 5.alpha.-reductase inhibitors for urinary tract disorder treatment)

L146 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2003:242003 CAPLUS

DOCUMENT NUMBER: 138:260465

TITLE: Pharmaceutical composition comprising receptor agonists and antagonists treatment of urinary disorder

INVENTOR(S): Arneric, Stephen P.; Andersson, Per-Olof

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 8 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003060513	A1	20030327	US 2001-965556	20010927
WO 2003026564	A2	20030403	WO 2002-SE1748	20020926

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,  
TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
NE, SN, TD, TG

## PRIORITY APPLN. INFO.:

US 2001-965556 A 20010927  
SE 2001-3858 A 20011120

AB The present invention concerns the field of urol. The invention provides a novel pharmaceutical compn., comprising a pharmaceutically effective combination of (i) a first compd. selected from the group consisting of muscarinic receptor antagonists, 5.alpha.-reductase inhibitors, and .alpha.-adrenergic receptor antagonists, and precursors and pharmaceutically acceptable salts thereof, and (ii) a second compd. selected from the group consisting of 5-HT1a receptor agonists and antagonists, and precursors and pharmaceutically acceptable salts thereof, and optionally a pharmaceutically acceptable carrier or diluent therefor. There is also provided a method of therapeutical treatment of urinary disorder in a mammal, including man, comprising administering to said mammal, including man, in need of such treatment, a therapeutically effective amt. of a compn. according to the invention. A pharmaceutical compn. contained between about 2 mg to about 20 mg of 5a-reductase inhibitor and between about 0.5 mg to about 50 mg of neutral 5-HT1a receptor antagonist. The compn. is administered to a patient for the treatment of urinary disorder.

IT 5633-20-5, Oxybutynin 124937-51-5,  
Tolterodine 133099-04-4, Darifenacin

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(pharmaceutical compn. comprising receptor agonists and antagonists  
treatment of urinary disorder)

L146 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2003 ACS.

ACCESSION NUMBER: 2001:185528 CAPLUS

DOCUMENT NUMBER: 134:242644

TITLE: Methods and compositions for preventing and treating  
urinary tract disorders

INVENTOR(S): Neal, Gary W.

PATENT ASSIGNEE(S): Androsolutions, Inc., USA

SOURCE: PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001017480	A2	20010315	WO 2000-US24685	20000908
WO 2001017480	A3	20011101		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1214039	A2	20020619	EP 2000-961687	20000908
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE,			

SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:

US 1999-152902P P 19990909

WO 2000-US24685 W 20000908

AB The present invention relates to methods, compns., devices and kits for the prevention and treatment of urinary tract disorders in mammals, including, but not limited to, urinary incontinence of any etiol., urinary hesitancy, fibrosis of the urinary tract, urinary dribbling, cystitis of any etiol., urinary frequency, and bladder cancer. The present invention provides methods for preventing and treating urinary tract disorders in mammals by administration of a therapeutic compd. to mucosal membranes in the lower urinary tract of the mammal. The present invention also provides devices for administering a therapeutic compd. to mucosal membranes in the lower urinary tract of the mammal. PGE-2 was added in a base matrix contg. tripalmitin and Me palmitate, and the mixt. was drawn into rigid tube made of high-d. polyethylene to obtain soft suppositories.

IT 5633-20-5, Oxybutynin 19237-84-4,  
Prazosin hydrochloride 74191-85-8, Doxazosin  
124937-51-5, Tolterodine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(treatment of urinary tract disorders by administering drug to mucosal membranes of lower urinary tract)

L146 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:608551 CAPLUS

DOCUMENT NUMBER: 133:213151

TITLE: Pharmaceutical compositions and methods for improved delivery of hydrophobic therapeutic agents

INVENTOR(S): Patel, Manesh V.; Chen, Feng-Jing

PATENT ASSIGNEE(S): Lipocine, Inc., USA

SOURCE: PCT Int. Appl., 98 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050007	A1	20000831	WO 2000-US165	20000105
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6294192	B1	20010925	US 1999-258654	19990226
NZ 513810	A	20010928	NZ 2000-513810	20000105
EP 1158959	A1	20011205	EP 2000-901394	20000105
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002537317	T2	20021105	JP 2000-600619	20000105

PRIORITY APPLN. INFO.:

US 1999-258654 A 19990226

WO 2000-US165 W 20000105

AB The present invention relates to triglyceride-free pharmaceutical compns. for delivery of hydrophobic therapeutic agents. Compns. of the present invention include a hydrophobic therapeutic agent and a carrier, where the carrier is formed from a combination of a hydrophilic surfactant and a hydrophobic surfactant. Upon diln. with an aq. solvent, the compn. forms a clear, aq. dispersion of the surfactants contg. the therapeutic agent. The invention also provides methods of treatment with hydrophobic

therapeutic agents using these compns. A pharmaceutical compn. contained cyclosporin 0.14, Cremophor RH-40 0.41, Arlacell186 0.29, sodium taurocholate 0.26, and propylene glycol 0.46 mg.

IT 63590-64-7, Terazosin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical compns. and methods for improved delivery of hydrophobic therapeutic agents)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L146 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:41675 CAPLUS

DOCUMENT NUMBER: 135:81

TITLE: New roles for muscarinic receptors in the pathophysiology of lower urinary tract symptoms

AUTHOR(S): Andersson, K.-E.

CORPORATE SOURCE: Department of Clinical Pharmacology, Lund University Hospital, Lund, Swed.

SOURCE: BJU International (2000), 86(Suppl. 2), 36-43  
CODEN: BJINFO; ISSN: 1464-4096

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 77 refs. The efficacy of both antimuscarinic drugs and .alpha.1-adrenoceptor antagonists in the treatment of lower urinary tract symptoms (LUTS) supports an important role for both muscarinic receptors and .alpha.1-adrenoceptors in the pathogenesis of the symptoms, and suggests that a combination of antimuscarinic drugs and .alpha.1-adrenoceptor antagonists may have treatment advantages.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L146 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:534795 CAPLUS

DOCUMENT NUMBER: 129:153255

TITLE: Controlled-release formulations for treating early morning pathologies

INVENTOR(S): Busetti, Cesare; Crimella, Tiziano

PATENT ASSIGNEE(S): Poli Industria Chimica Spa, Italy

SOURCE: U.S., 9 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5788987	A	19980804	US 1997-790514	19970129
WO 9832425	A1	19980730	WO 1997-IB1632	19971216
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9853356	A1	19980818	AU 1998-53356	19971216
EP 954292	A1	19991110	EP 1997-950352	19971216
R:	BE, DE, ES, FR, GB, PT			
JP 2001511126	T2	20010807	JP 1998-531769	19971216
			US 1997-790514	A 19970129

PRIORITY APPLN. INFO.:

WO 1997-IB1632 W 19971216

AB Early morning pathologies are treated by use of a time-specific controlled-release dosage formulation which is administered prior to sleep; the formulation delivers a pharmaceutically active agent effective for treatment of the pathol. at about the time of awakening. The formulation comprises a core contg. the drug and a swellable polymeric coating layer surrounding the core. The swellable polymeric coating layer delays the release of the drug from the core for a predetd. period of time dependent on the thickness of the layer, to effect delivery of the drug at about the time of awakening. Early morning pathologies include asthma, angina, hypertension, myocardial or cerebral infarction, arthritis, incontinence, parkinsonism, and sleep disorders. Thus, a granular mixt. of diclofenac Na 25, CaHPO<sub>4</sub>·2H<sub>2</sub>O 94.5, microcryst. cellulose 113, tartaric acid 25, NaHCO<sub>3</sub> 25,, colloidal SiO<sub>2</sub> 1.5, and Mg stearate 1 wt. parts was pressed into 285-mg tablet cores and coated with an aq. soln. contg. hydroxypropylmethylcellulose 7.5 and PEG-6000 1.5 wt.% until the coating wt. was 50% of the core wt. The coated tablets showed a dissoln. time lag >300 min, followed by quick disintegration.

IT 5633-20-5, Oxybutynin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled-release formulations for treating early morning pathologies)

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L146 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:525366 CAPLUS

DOCUMENT NUMBER: 125:211656

TITLE: Analysis of pressure/flow characteristics in the female rat and their pharmacologic modulation

AUTHOR(S): Watanabe, Takeshi; Constantinou, Christos E.

CORPORATE SOURCE: Department Urology, Tottori University, Yonago, Japan

SOURCE: Neurourology and Urodynamics (1996), 15(5), 513-527

CODEN: NEUREM; ISSN: 0733-2467

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new in vivo urodynamic animal model was developed to analyze the micturition characteristics of the rat. This model was used to study the modulating effect of pharmacol. agents on vesicourethral function, using cystometry and uroflowmetry. Pressure-flow studies were done in 25 female rats anesthetized with urethane. Filling cystometry was recorded using a physiol. rate of bladder filling through transvesical infusion. Micturition characterization was done by identifying the time course and amt. of voided vol. Voided vol. was measured by a novel application of a mechanotransducer, which provided the data to measure flow rate and compute the voided vol.-time curve. Flow rate was calcd. by differentiating the curve produced by the mechanotransducer. Using this system, comparative tests of pharmacol. stimulus were done using anticholinergic stimulation, .alpha.1 blocker, and a new N-methyl-D-aspartate (NMDA) receptor antagonist. The effects of the i.v. use of these drugs in the lower urinary tract were evaluated at various dose levels. The results showed that anticholinergic stimulation produced an increase of bladder capacity and decreases of detrusor pressure and max. flow rate. Although the .alpha.1 blocker decreased detrusor pressure, flow rate did not change significantly. By contrast, NMDA receptor antagonism produced a depressant effect on bladder reflex contraction, and increased bladder capacity in a dose-dependent way. However, max. flow rate increased at a dose of 10 mg/kg and decreased at 30 mg/kg significantly. These results suggest that a decrease in flow resistance through the outlet region was due to the effects of NMDA

receptor inhibition at lower doses. In conclusion, this model enables the evaluation of drugs regarding lower urinary tract function and provides in small animals the possibility of evaluating the relationships between pressure and flow in various exptl. models.

IT 1508-65-2, Oxybutynin chloride 19216-56-9,

Prazosin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(urodynamic animal model to analyze micturition and its pharmacol. characterization)

L146 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:73296 CAPLUS

DOCUMENT NUMBER: 124:97773

TITLE: Percutaneously administrable preparation for treating urination disorder

INVENTOR(S): Nakamura, Katsuhiro; Koga, Nobuyuki

PATENT ASSIGNEE(S): Hisamitsu Pharmaceutical Co., Inc., Japan

SOURCE: PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9531190	A1	19951123	WO 1995-JP946	19950518
W: AU, CA, CN, JP, KR, US, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9524544	A1	19951205	AU 1995-24544	19950518
EP 760238	A1	19970305	EP 1995-918735	19950518
EP 760238	B1	20020417		
R: CH, DE, DK, ES, FR, GB, IE, IT, LI, NL				
ES 2172584	T3	20021001	ES 1995-918735	19950518
US 5770221	A	19980623	US 1996-737160	19961115
PRIORITY APPLN. INFO.:			JP 1994-128162	A 19940518
			WO 1995-JP946	W 19950518

AB A percutaneously administrable prepn. for treating urination disorder comprises a remedy for urination disorder and a pressure-sensitive adhesive contg. low- and high-mol.-wt. polyisobutylenes and a fat or oil as the principal base; and another such prepn. comprises a remedy for urination disorder and a pressure-sensitive adhesive contg. low- and high-mol.-wt. polyisobutylenes, a fat or oil and a styrene-isoprene-styrene block copolymer as the principal base. These preps., contg. the above-specific base component, are excellent in stability even after the lapse of time, lowly irritative to the skin, and excellent in percutaneous absorbability. As an example, high-mol.-wt. polyisobutylene 15.5, low-mol.-wt. polyisobutylene 16.5, squalane 45.0, hydrogenated rosin esters 10.0 and pepper oil 3.0 wt. parts were dissolved in hexane, mixed with oxybutynin, and spread on a separable sheet, which was placed on a polyester film to give a percutaneous prepn.

IT 1508-65-2, Oxybutynin hydrochloride 5633-20-5,

Oxybutynin 19216-56-9, Prazosin

63590-64-7, Terazosin

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Percutaneously administrable prepn. for treating urination disorder)

L146 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:499511 CAPLUS

DOCUMENT NUMBER: 121:99511

TITLE: Effects of intravesically administered

Searched by Barb O'Bryen, STIC 308-4291

anticholinergics, a .beta.-adrenergic stimulant and an .alpha.-adrenergic blocker on bladder function in unanesthetized rats

AUTHOR(S): Ukimura, Osamu  
CORPORATE SOURCE: Dep. Urol., Kyoto Prefect. Univ. Med., Kyoto, 602, Japan  
SOURCE: Tohoku Journal of Experimental Medicine (1993), 170(4), 251-60  
CODEN: TJEMAO; ISSN: 0040-8727  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Comparative anal. of the effects of intravesical instillation of the title drugs on urodynamic parameters was performed in unanesthetized rats. The drugs were atropine (7.2 .times. 10-4-7.2 .times. 10-2M), propantheline (7.2 .times. 10-3-2.2 .times. 10-2M), oxybutynin (2.5 .times. 10-3-2.5 .times. 10-2M), isoproterenol (5 .times. 10-2-10-1M) and prazosin (5 .times. 10-4M). These intravesical drugs suppressed spontaneous bladder contractions and changed micturition function in the urinary filling and storage phases.

IT 5633-20-5, Oxybutynin 19216-56-9,  
Prazosin  
RL: BIOL (Biological study)  
(bladder function response to)

L146 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 1993:420336 CAPLUS  
DOCUMENT NUMBER: 119:20336  
TITLE: Effects of drugs used in the therapy of detrusor hyperactivity on the volume-induced contractions of the rat urinary bladder

AUTHOR(S): Guarneri, L.; Ibba, M.; Angelico, P.; Colombo, D.; Fredella, B.; Testa, R.  
CORPORATE SOURCE: Pharmacol. Dep., Recordati S.p.A., Milan, 20148, Italy  
SOURCE: Pharmacological Research (1993), 27(2), 173-87  
CODEN: PHMREP; ISSN: 1043-6618  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In this study, the authors examd. the effects of the drugs most commonly utilized in the therapy of overactive detrusor, on the vol.-induced contractions of rat urinary bladder. Anticholinergics such as propantheline bromide and emepronium bromide, as well as oxybutynin decreased the amplitude of the voiding contractions after i.v. administration in a dose-dependent way. These anticholinergics, on the other hand, generally increased the frequency of the contractions. Nifedipine dose-dependently reduced the amplitude of the contractions. Flavoxate induced a dose-related decrease in the frequency without effects on the amplitude of the peaks. Its main metabolite 3-methylflavone-8-carboxylic acid (MFCA) was inactive after i.v. administration. Terodiline was active on the amplitude and apparently on the frequency of the voiding contractions. The .alpha.-adrenoceptor antagonist prazosin, as well as indomethacin, inhibited only the frequency of the voiding contractions. All the drugs active in reducing the frequency of the voiding contractions after i.v. administration, proved effective also after intracerebroventricular (i.c.v.) injection. The model of the vol.-induced contractions of rat urinary bladder, seems to be a useful tool to evaluate in vivo the effects of a compd. on the bladder, allowing the possibility of distinguishing among antimuscarinics and calcium antagonists, which peripherally decrease bladder contractility, and other drugs inducing a decrease in the frequency of the voiding reflex acting on the micturition centers in the CNS.

IT 5633-20-5, Oxybutynin 19216-56-9,  
Prazosin  
RL: BIOL (Biological study)

(urinary bladder contraction response to, detrusor hyperactivity treatment in relation to)

L146 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1982:574990 CAPLUS

DOCUMENT NUMBER: 97:174990

TITLE: Direct measurement of the anticholinergic activity of

a series of pharmacological compounds on the canine and rabbit urinary bladder

AUTHOR(S): Levin, Robert M.; Wein, Alan J.

CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, Philadelphia, PA, USA

SOURCE: Journal of Urology (Hagerstown, MD, United States)

(1982), 128(2), 396-8

CODEN: JOURAA; ISSN: 0022-5347

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The relative potency of a variety of drugs to compete for muscarinic cholinergic receptors isolated from the canine and rabbit urinary bladder was detd. Radio-ligand binding assays for muscarinic receptors were performed with 10 nM 3H-labeled quinuclidinyl benzilate and various concns. of the drugs under study. Of the agents tested propantheline (I) [298-50-0], atropine [51-55-8], and glycopyrrolate [596-51-0] were the potent muscarinic antagonists/unit of concn. oxybutynin [5633-20-5] And dicyclomine [77-19-0] were 30 to 50 times less potent than atropine. chlorpromazine [50-53-3] And desmethylinipramine [50-47-5] were approx. 500 times less potent than atropine. Agents such as guanethidine [55-65-2], tranylcypromine [155-09-9], and hexamethonium [60-26-4] possessed little antimuscarinic activity.

IT 5633-20-5 19216-56-9

RL: BIOL (Biological study)

(antimuscarinic activity of, bladder response in relation to)

L146 ANSWER 14 OF 35

MEDLINE

DUPLICATE 3

ACCESSION NUMBER: 1999321789 MEDLINE

DOCUMENT NUMBER: 99321789 PubMed ID: 10393480

TITLE: Pharmacological management of incontinence.

AUTHOR: Sullivan J; Abrams P

CORPORATE SOURCE: Bristol Urological Institute, Southmead Hospital, Bristol,

UK.. edu@bui.ac.uk

SOURCE: EUROPEAN UROLOGY, (1999) 36 Suppl 1 89-95. Ref: 29

Journal code: 7512719. ISSN: 0302-2838.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199907

ENTRY DATE: Entered STN: 19990816

Last Updated on STN: 19990816

Entered Medline: 19990730

#### ABSTRACT:

Many patients with incontinence do not need surgery - for these patients symptoms can often be considerably improved by conservative measures, including drugs. Several different pharmacological actions are potentially useful depending on the underlying cause of the incontinence: a) Detrusor instability (DI) responds to drugs reducing bladder contractility: Anticholinergic agents, e.g. **oxybutynin** and **tolterodine**, act at postganglionic parasympathetic cholinergic receptor sites on the detrusor muscle, reducing the strength of the detrusor contraction. Tricyclic antidepressants, e.g.

imipramine, have anticholinergic effects, block presynaptic uptake of amine neurotransmitters and directly inhibit detrusor muscle. Alpha-adrenergic antagonists may have a role to play by dual actions on bladder overactivity (due to altered receptor function) and by reducing outlet resistance. b) Genuine stress incontinence (GSI) may be treated using alpha-adrenergic agonists, e.g. phenylpropanolamine, to increase outlet resistance by stimulating smooth muscle of the urethra and bladder neck. c) In nocturnal enuresis reduction of nocturnal urine output with the anti-diuretic hormone (ADH) analogue DDAVP (1-deamino, 8-arginine vasopressin) is beneficial. d) Bladder emptying may be facilitated in patients with retention and 'overflow' incontinence by alpha-adrenergic antagonists, which reduce outlet resistance, and perhaps by parasympathomimetics, e.g. bethanecol. e) In postmenopausal women, systemic oestrogen replacement reduces filling symptoms including urge incontinence. Evidence for oestrogen replacement alone in GSI is lacking, but combination with alpha-agonists is beneficial in milder GSI. For the future, \*\*\*tolterodine\*\*\* and other new anticholinergics offer the hope of treatment for DI with fewer of the side effects that limit the use of established drugs. Better understanding of the pathophysiology of DI may provide new targets for drug therapy, such as hyperpolarisation of detrusor muscle membrane. Alpha-agonists may find a greater role in the future, as may ADH analogues for nocturnal symptoms.

CONTROLLED TERM: Check Tags: Human  
Adrenergic alpha-Agonists: TU, therapeutic use  
**Adrenergic alpha-Antagonists: TU, therapeutic use**  
**Bladder: DE, drug effects**  
Cholinergic Antagonists: TU, therapeutic use  
\*Urinary Incontinence: DT, drug therapy  
Urinary Incontinence: ET, etiology  
Urinary Incontinence: PP, physiopathology  
Urinary Incontinence, Stress: DT, drug therapy  
Urinary Incontinence, Stress: PP, physiopathology

CHEMICAL NAME: 0 (Adrenergic alpha-Agonists); 0 (Adrenergic alpha-Antagonists); 0 (Cholinergic Antagonists)

L146 ANSWER 15 OF 35 MEDLINE  
ACCESSION NUMBER: 2003166117 MEDLINE  
DOCUMENT NUMBER: 22570270 PubMed ID: 12683100  
TITLE: Managing lower urinary tract symptoms in men.  
AUTHOR: Anonymous  
SOURCE: DRUG AND THERAPEUTICS BULLETIN, (2003 Mar) 41 (3) 18-21.  
Journal code: 0112037. ISSN: 0012-6543.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200305  
ENTRY DATE: Entered STN: 20030410  
Last Updated on STN: 20030520  
Entered Medline: 20030519

**ABSTRACT:**

Over one-quarter of men aged 40 years or over in the UK have lower urinary tract symptoms. These symptoms, which may seriously disrupt day-to-day activity, include frequency, urgency, hesitancy, reduced flow, dribbling, nocturia, incontinence and incomplete emptying of the bladder. Here, we review non-surgical measures that may help men with such symptoms.

CONTROLLED TERM: Check Tags: Human; Male  
**Adrenergic alpha-Antagonists: TU, therapeutic use**  
Adult  
Aged  
Enzyme Inhibitors: AD, administration & dosage  
Middle Age  
**Muscarinic Antagonists: TU, therapeutic use**  
Phytotherapy: MT, methods

**Prostatic Hyperplasia: CO, complications**  
**\*Prostatic Hyperplasia: DT, drug therapy**  
Referral and Consultation  
Testosterone 5-alpha-Reductase: AI, antagonists & inhibitors

CHEMICAL NAME: \*Urinary Retention: DT, drug therapy  
Urinary Retention: ET, etiology  
0 (Adrenergic alpha-Antagonists); 0 (Enzyme Inhibitors); 0 (Muscarinic Antagonists); EC 1.3.99.5 (Testosterone 5-alpha-Reductase)

L146 ANSWER 16 OF 35 MEDLINE  
ACCESSION NUMBER: 1998266593 MEDLINE  
DOCUMENT NUMBER: 98266593 PubMed ID: 9605556  
TITLE: The adrenergic, cholinergic and NANC nerve-mediated contractions of the female rabbit bladder neck and proximal, medial and distal urethra.  
AUTHOR: Deplanne V; Palea S; Angel I  
CORPORATE SOURCE: Synthelabo Recherche, Department of Internal Medicine, Rueil-Malmaison, France.  
SOURCE: BRITISH JOURNAL OF PHARMACOLOGY, (1998 Apr) 123 (8) 1517-24.  
Journal code: 7502536. ISSN: 0007-1188..  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199807  
ENTRY DATE: Entered STN: 19980716  
Last Updated on STN: 19980716  
Entered Medline: 19980707

## ABSTRACT:

1. The nerve-mediated contraction of the female rabbit bladder neck and different portions of the urethra (proximal, medial and distal) was studied in vitro by electrical stimulation (50 V, 30 Hz, 0.05 ms width, trains of 5 s every 5 min) by use of a superfusion system. 2. The amplitude (Emax) and the duration (Dmax) of the stimulated contraction were studied in the four tissues. The Emax value was significantly higher in distal urethra (2.07+/-0.15 g) compared to the bladder neck (1.08+/-0.10 g), proximal urethra (0.73+/-0.07 g) and medial urethra (0.87+/-0.07 g). In contrast, the Dmax value appeared slightly but significantly lower (P<0.05) in distal urethra (68.5+/-2.3 s) than in bladder neck (76.7+/-6.0 s), proximal urethra (84.5+/-5.0 s) and medial urethra (81.3+/-3.5 s). 3. Cocaine (1 microM) significantly increased the basal Emax values in medial and distal urethra and the basal Dmax values in the four tissues. 4. Prazosin (1 microM) significantly reduced E max value in proximal, medial and distal urethra and Dmax value in bladder neck and proximal urethra. Atropine (1 microM) also significantly reduced Emax values in bladder neck and proximal urethra and reduced Dmax value in bladder neck, but not in other tissues. Yohimbine (0.1 microM) was devoid of effect in the four tissues. 5. The association of prazosin (1 microM) and atropine (1 microM) did not modify the Emax and the Dmax values of the electrically-induced contractions, except in proximal urethra and in bladder neck where an additive inhibitory effect (on Emax only) was observed compared to prazosin and atropine alone. 6. The residual contractile response after combined treatment with prazosin and atropine was significantly diminished by tetrodotoxin (TTX; 1 microM) but not completely abolished. These NANC contractions were insensitive to P2X-purinoceptor desensitization by continuous tissue perfusion with alpha,beta-methylene ATP (30 microM). 7. These results demonstrate that bladder neck and proximal urethra are mainly innervated by the parasympathetic nervous system, whereas medial and distal urethras are to a greater extent under the control of the sympathetic innervation. The residual responses, insensitive to prazosin and atropine, may indicate a NANC innervation in the four tissues. However, the nature of the NANC neurotransmitter remains to be

identified.

CONTROLLED TERM: Check Tags: Animal; Female; In Vitro  
Adrenergic alpha-Antagonists: PD, pharmacology  
Atropine: PD, pharmacology  
\*Autonomic Nervous System: PH, physiology  
Bladder: IR, innervation  
\*Bladder: PH, physiology  
Cocaine: PD, pharmacology  
Electric Stimulation  
Muscarinic Antagonists: PD, pharmacology  
Muscle Contraction: PH, physiology  
\*Muscle, Smooth: PH, physiology  
Neurotransmitters: ME, metabolism  
Parasympathetic Nervous System: PH, physiology  
Prazosin: PD, pharmacology  
Rabbits  
Sympathetic Nervous System: PH, physiology  
Urethra: IR, innervation  
\*Urethra: PH, physiology  
Vasoconstrictor Agents: PD, pharmacology  
Yohimbine: PD, pharmacology  
CAS REGISTRY NO.: 146-48-5 (Yohimbine); 19216-56-9 (Prazosin);  
50-36-2 (Cocaine); 51-55-8 (Atropine)  
CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Muscarinic  
Antagonists); 0 (Neurotransmitters); 0 (Vasoconstrictor  
Agents)

L146 ANSWER 17 OF 35 MEDLINE  
ACCESSION NUMBER: 97319457 MEDLINE  
DOCUMENT NUMBER: 97319457 PubMed ID: 9176360  
TITLE: Reflex pathways controlling urethral striated and smooth  
muscle function in the male rat.  
AUTHOR: Kakizaki H; Fraser M O; De Groat W C  
CORPORATE SOURCE: Department of Pharmacology, University of Pittsburgh School  
of Medicine, Pennsylvania 15261, USA.  
CONTRACT NUMBER: DK-49430 (NIDDK)  
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1997 May) 272 (5 Pt 2)  
R1647-56.  
Journal code: 0370511. ISSN: 0002-9513.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199706  
ENTRY DATE: Entered STN: 19970716  
Last Updated on STN: 19970716  
Entered Medline: 19970627

ABSTRACT:

The organization of vesicourethral reflex mechanisms in the male rat was studied by monitoring intraurethral pressure and the external urethral sphincter (EUS) electromyogram. EUS striated and urethral smooth muscle activities were elicited by reflex isovolumetric bladder contractions evoked by bladder filling or electrical stimulation of nerves in the bladder wall. Evoked EUS bursting activity in normal rats was eliminated in chronic spinal rats and replaced by tonic activity. Reflex urethral smooth muscle activity mediated by an increase in urethral pressure after paralysis of the EUS with alpha-bungarotoxin occurred in normal and chronic spinal rats. The response was significantly larger in chronic spinal (21.3 +/- 3.0 cmH2O) than in normal rats (4.2 +/- 0.7 cmH2O). NG-nitro-L-arginine methyl ester (a nitric oxide synthase inhibitor, 20 mg/kg i.v.) increased the smooth muscle response in normal (5.9 +/- 1.3 cmH2O) and chronic spinal rats (6.9 +/- 1.8 cmH2O). This increase in urethral pressure was not changed by sympathetic nerve transection or prazosin (0.2-0.3 mg/kg i.v.) but was abolished by hexamethonium and reduced

74-89% by atropine. These results indicate that coordinated EUS function (bursting activity) in the male rat is dependent on supraspinal pathways and that the urethral smooth muscle response during voiding is composed of a predominant cholinergic, atropine-sensitive contraction as well as a nitric oxide-mediated relaxation. Both are mediated by activation of parasympathetic pathways and are maintained or significantly larger after spinal cord injury, indicating that they are dependent on spinal reflex pathways.

CONTROLLED TERM: Check Tags: Animal; Female; Male; Support, U.S. Gov't, P.H.S.

**Adrenergic alpha-Antagonists: PD, pharmacology**

Atropine: PD, pharmacology

**\*Bladder: PH, physiology**

Denervation

Electromyography

Hydrostatic Pressure

**Muscarinic Antagonists**

Muscle, Smooth: PH, physiology

NG-Nitroarginine Methyl Ester: PD, pharmacology

Parasympathetic Nervous System: PH, physiology

**Prazosin: PD, pharmacology**

Rats

Reflex

Sex Factors

**\*Urethra: PH, physiology**

**Urination**

CAS REGISTRY NO.: 19216-56-9 (Prazosin); 50903-99-6  
(NG-Nitroarginine Methyl Ester); 51-55-8 (Atropine)  
CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Muscarinic Antagonists)

L146 ANSWER 18 OF 35 MEDLINE

ACCESSION NUMBER: 96312683 MEDLINE

DOCUMENT NUMBER: 96312683 PubMed ID: 8740024

TITLE: Evidence of nonadrenergic, noncholinergic contraction in rat urinary bladder by 1,1-dimethylphenylpiperazinium stimulation in vivo.

AUTHOR: Tong Y C; Hung Y C; Cheng J T

CORPORATE SOURCE: Department of Urology, National Cheng Kung University, Medical College, Tainan, Taiwan/ROC.

SOURCE: EUROPEAN UROLOGY, (1996) 29 (3) 362-5.  
Journal code: 7512719. ISSN: 0302-2838.

PUB. COUNTRY: Switzerland

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199610

ENTRY DATE: Entered STN: 19961022

Last Updated on STN: 19961022

Entered Medline: 19961008

**ABSTRACT:**

Nonadrenergic, noncholinergic (NANC) contraction has been demonstrated in animal urinary bladder. However, the exact nature of the NANC innervation is still unclear. 1,1-Dimethylphenylpiperazinium (DMPP), which generates action potentials in the cell body of the postganglionic neuron and causes neurotransmitter release (both acetylcholine and noradrenaline), was given intravenously (0.1-0.7 mg/kg) to 3-month-old female Wistar rats under anesthesia (n = 20). Intravesical pressure, heart rate and blood pressure of the rats were monitored on Gould polygraph. Monophasic dose-dependent contractile response was observed upon administration of DMPP in 12 of 20 rats. After total adrenergic and cholinergic blockade with atropine, guanethidine, phentolamine and propranolol, the contractile response was reduced, not completely, in the animals. At the dose of 0.7 mg/kg, the contraction was reduced to about 48% of the original response. The study provides in vivo

evidence for NANC contraction in the rat urinary bladder, moreover, the neurotransmitter is released from the postganglionic neurons.

CONTROLLED TERM: Check Tags: Animal; Female; Support, Non-U.S. Gov't  
Action Potentials: DE, drug effects  
Adrenergic Agents: AD, administration & dosage  
Adrenergic Agents: PD, pharmacology  
Atropine: AD, administration & dosage  
Atropine: PD, pharmacology  
\*Bladder: DE, drug effects  
Dimethylphenylpiperazinium Iodide: AD, administration & dosage  
dosage  
\*Dimethylphenylpiperazinium Iodide: PD, pharmacology  
Dose-Response Relationship, Drug  
Drug Interactions  
Ganglionic Stimulants: AD, administration & dosage  
\*Ganglionic Stimulants: PD, pharmacology  
Guanethidine: AD, administration & dosage  
Guanethidine: PD, pharmacology  
Injections, Intravenous  
Muscle Contraction: DE, drug effects  
\*Muscle, Smooth: DE, drug effects  
Neurons: CY, cytology  
Neurons: DE, drug effects  
Nicotinic Agonists: AD, administration & dosage  
\*Nicotinic Agonists: PD, pharmacology  
Phentolamine: AD, administration & dosage  
Phentolamine: PD, pharmacology  
Propranolol: AD, administration & dosage  
Propranolol: PD, pharmacology  
Rats  
Rats, Wistar  
Synaptic Transmission: DE, drug effects  
CAS REGISTRY NO.: 50-60-2 (Phentolamine); 51-55-8 (Atropine); 525-66-6  
(Propranolol); 54-77-3 (Dimethylphenylpiperazinium Iodide);  
55-65-2 (Guanethidine)  
CHEMICAL NAME: 0 (Adrenergic Agents); 0 (Ganglionic Stimulants); 0  
(Nicotinic Agonists)

L146 ANSWER 19 OF 35 MEDLINE  
ACCESSION NUMBER: 96162560 MEDLINE  
DOCUMENT NUMBER: 96162560 PubMed ID: 8583354  
TITLE: Analysis of the mechanisms underlying the contractile  
response induced by the hydroalcoholic extract of  
Phyllanthus urinaria in the guinea-pig urinary bladder  
in-vitro.  
AUTHOR: Dias M A; Campos A H; Cechinel Filho V; Yunes R A; Calixto  
J B  
CORPORATE SOURCE: Department of Pharmacology, Universidade Federal de Santa  
Catarina, Florianopolis SC, Brazil.  
SOURCE: JOURNAL OF PHARMACY AND PHARMACOLOGY, (1995 Oct) 47 (10)  
846-51.  
Journal code: 0376363. ISSN: 0022-3573.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199603  
ENTRY DATE: Entered STN: 19960327  
Last Updated on STN: 19980206  
Entered Medline: 19960315

ABSTRACT:  
The hydroalcoholic extract of Phyllanthus urinaria (Euphorbiaceae), substance P  
and substance P methyl ester all caused graded contractions in the guinea-pig

urinary bladder. Responses to hydroalcoholic extract and substance P were markedly inhibited in calcium-free Krebs solution, this effect being reversed by reintroduction of calcium in the medium. The contraction in response to hydroalcoholic extract was unaffected by atropine, propranolol, prazosin, yohimbine, tetrodotoxin, w-conotoxin, nicardipine, HOE 140, guanethidine, staurosporine, phorbol ester or indomethacin, excluding the involvement of nervous mediated responses, or action via cholinergic, adrenergic, kinins, cyclo-oxygenase metabolites, protein kinase C or activation of L or N-type calcium channels. The selective NK1 tachykinin antagonist (FK 888), but not NK2 (SR 48968) antagonized substance P-induced contraction, but both drugs failed to effect Phyllanthus urinaria-induced contraction. Prolonged desensitization of guinea pig urinary bladder with capsaicin (10 microM) or preincubation of guinea-pig urinary bladder with capsazepine did not affect contraction caused by hydroalcoholic extract. Ruthenium red almost completely abolished capsaicin-induced contraction, but had no effect on hydroalcoholic extract-mediated contraction. Substance P and the hydroalcoholic extract caused marked potentiation of the twitch response in the preparations field stimulated. The facilitatory effect of substance P, but not that of hydroalcoholic extract, was prevented by the NK1 (FK 888), but not by NK2 (SR 48968) antagonist. We concluded that contraction induced by hydroalcoholic extract of Phyllanthus urinaria in the guinea pig urinary bladder involves direct action on smooth muscle and relies on the mobilization of extracellular calcium influx unrelated to activation of L- and N-type calcium channels or activation of protein kinase C mechanisms. In addition contraction caused by the hydroalcoholic extract of Phyllanthus urinaria in guinea-pig urinary bladder does not involve the activation of tachykinin or vanilloid receptors.

CONTROLLED TERM: Check Tags: Animal; Female; In Vitro; Male; Support,  
Non-U.S. Gov't

**Adrenergic alpha-Antagonists:** PD, pharmacology

Adrenergic beta-Antagonists: PD, pharmacology

Benzamides: PD, pharmacology

**\*Bladder:** DE, drug effects

**Bladder:** PH, physiology

Dipeptides: PD, pharmacology

Ethanol: CH, chemistry

Guinea Pigs

Indoles: PD, pharmacology

Ion Channels: DE, drug effects

**Muscarinic Antagonists:** PD, pharmacology

\*Muscle Contraction: DE, drug effects

Muscle, Smooth: DE, drug effects

Muscle, Smooth: PH, physiology

Neurokinin A: AI, antagonists & inhibitors

Piperidines: PD, pharmacology

\*Plant Extracts: PD, pharmacology

Plants, Medicinal

Receptors, Tachykinin: AI, antagonists & inhibitors

Substance P: AI, antagonists & inhibitors

Substance P: PD, pharmacology

CAS REGISTRY NO.: 138449-07-7 (FK 888); 142001-63-6 (SR 48968); 33507-63-0  
(Substance P); 64-17-5 (Ethanol); 86933-74-6 (Neurokinin A)

CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Adrenergic  
beta-Antagonists); 0 (Benzamides); 0 (Dipeptides); 0  
(Indoles); 0 (Ion Channels); 0 (Muscarinic Antagonists); 0  
(Piperidines); 0 (Plant Extracts); 0 (Receptors,  
Tachykinin)

L146 ANSWER 20 OF 35

MEDLINE

ACCESSION NUMBER: 93247154 MEDLINE

DOCUMENT NUMBER: 93247154 PubMed ID: 8387116

TITLE: Control of detrusor stiffness in the chronic decentralized  
feline bladder.

AUTHOR: Skehan A M; Downie J W; Awad S A

Searched by Barb O'Bryen, STIC 308-4291

CORPORATE SOURCE: Department of Urology, Dalhousie University, Halifax, Nova Scotia, Canada.  
SOURCE: JOURNAL OF UROLOGY, (1993 May) 149 (5) 1165-73.  
Journal code: 0376374. ISSN: 0022-5347.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199305  
ENTRY DATE: Entered STN: 19930618  
Last Updated on STN: 19930618  
Entered Medline: 19930528

## ABSTRACT:

The neuropharmacology of increased bladder stiffness, which may contribute to upper tract damage and incontinence, was investigated in 76 cats. beta-blockade increased but combined alpha 1-adrenergic with muscarinic blockade decreased filling phase stiffness in normal cats. Bladder wall stiffness during the early filling phase was unaffected by chronic S2 ventrodorsal rhizotomy or L7-S3 ventral rhizotomy, but was decreased when L7-S3 dorsal rhizotomy or total sympathectomy was combined with the ventral root lesion, implying that sacral dorsal roots and sympathetic efferents maintain normal detrusor stiffness. Acute sympathectomy increased stiffness in all the former 3 chronic groups, implying that a tonic or reflex sympathetic inhibition operates independently of the L7-S3 dorsal roots. Stiffness during early filling phase decreased with acute ventral rhizotomy. This change persisted with chronic sympathectomy but returned to normal if sympathetic nerves were left intact. These results suggest that bladder stiffness is modulated by tonic or reflexic sympathetic activity, which is influenced by L7-S3 afferents. Detrusor stiffness during the later stages of filling, which was decreased by acute sympathectomy in chronic groups but increased by chronic sympathectomy, was reduced by interference with adrenergic or muscarinic mechanisms after either lesion. Therefore, a peripheral pathway with facilitatory alpha 1-adrenergic and muscarinic receptors is involved in the production of increased late stage stiffness after chronic sympathetic damage. We propose that the increased bladder stiffness seen in congenital sacral lesions may be analogous to the stiffness during late stages of filling reported here. Our results also imply that the presence of this increased stiffness is closely associated with chronic sympathetic damage. Whether the increased stiffness in congenital and traumatic neural lesions in humans arises from sympathetic damage remains to be determined.

CONTROLLED TERM: Check Tags: Animal; Male; Support, Non-U.S. Gov't

Atropine: PD, pharmacology

Bladder: IR, innervation

\*Bladder: PH, physiology

Cats

\*Denervation

Muscarinic Antagonists

Prazosin: PD, pharmacology

Receptors, Adrenergic, alpha: PH, physiology

Receptors, Muscarinic: PH, physiology

Spinal Nerve Roots: SU, surgery

Sympathectomy

\*Urodynamics

Urodynamics: DE, drug effects

CAS REGISTRY NO.: 19216-56-9 (Prazosin); 51-55-8 (Atropine)

CHEMICAL NAME: 0 (Muscarinic Antagonists); 0 (Receptors, Adrenergic, alpha); 0 (Receptors, Muscarinic)

L146 ANSWER 21 OF 35 MEDLINE

ACCESSION NUMBER: 91192889 MEDLINE

DOCUMENT NUMBER: 91192889 PubMed ID: 1672862

TITLE: DuP 753 is a specific antagonist for the angiotensin receptor.

AUTHOR: Rhaleb N E; Rouissi N; Nantel F; D'Orleans-Juste P; Regoli D  
CORPORATE SOURCE: Department of Pharmacology, Medical School University of Sherbrooke, Quebec, Canada.  
SOURCE: HYPERTENSION, (1991 Apr) 17 (4) 480-4.  
Journal code: 7906255. ISSN: 0194-911X.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199105  
ENTRY DATE: Entered STN: 19910602  
Last Updated on STN: 19980206  
Entered Medline: 19910513

## ABSTRACT:

2-n-Butyl-4-chloro-5-hydroxy-methyl-1-[(2'-(1H)-tetrazol-5-yl)biph enyl-4-yl)methyl]imidazol potassium salt (DuP 753) is a nonpeptide angiotensin II receptor antagonist that inhibits the contractile effects of angiotensin II competitively and shows pA2 values of 8.27 on the rabbit aorta and jugular vein, 8.66 on the rat portal vein and stomach, 8.19 on the rat urinary bladder, and 8.36 on human colon, ileum, and urinary bladder. This agent (more than 10(-5) M) exhibits no agonistic activity and does not affect the contractile effects of norepinephrine, acetylcholine, bradykinin, desArg9-bradykinin, substance P, neurokinin A, neurokinin B, or bombesin in the various tissues. The present results demonstrate that DuP 753 is a potent nonpeptide antagonist with high affinity, specificity, and selectivity for the angiotensin receptor.

CONTROLLED TERM: Check Tags: Animal; Human; In Vitro; Male; Support, Non-U.S. Gov't

**Adrenergic alpha-Antagonists: AI, antagonists & inhibitors**

Adult

\*Angiotensin II: AI, antagonists & inhibitors

**Bladder: DE, drug effects**

Blood Vessels: DE, drug effects

Digestive System: DE, drug effects

Imidazoles: AI, antagonists & inhibitors

\*Imidazoles: PD, pharmacology

Kinetics

Kinins: PD, pharmacology

Losartan

**Muscarinic Antagonists**

Rabbits

Rats

Rats, Inbred Strains

\*Receptors, Angiotensin: AI, antagonists & inhibitors

Tetrazoles: AI, antagonists & inhibitors

\*Tetrazoles: PD, pharmacology

CAS REGISTRY NO.: 11128-99-7 (Angiotensin II); 114798-26-4 (Losartan)

CHEMICAL NAME: 0 (Adrenergic alpha-Antagonists); 0 (Imidazoles); 0 (Kinins); 0 (Muscarinic Antagonists); 0 (Receptors, Angiotensin); 0 (Tetrazoles)

L146 ANSWER 22 OF 35

MEDLINE

ACCESSION NUMBER: 83111481 MEDLINE

DOCUMENT NUMBER: 83111481 PubMed ID: 6296355

TITLE: Characterization of the effect of quinidine on Na transport by the toad and turtle bladders.

AUTHOR: Arruda J A

CONTRACT NUMBER: AM20170 (NIADDK)

SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1983 Feb) 224 (2) 297-301.

Journal code: 0376362. ISSN: 0022-3565.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198303  
ENTRY DATE: Entered STN: 19900318  
Last Updated on STN: 19970203  
Entered Medline: 19830317

## ABSTRACT:

Quinidine inhibits Na transport by the toad and turtle bladder. This effect of quinidine is thought to be mediated by an increase in cytosolic calcium. In the present study, we characterized the effect of quinidine on Na transport by the toad and turtle bladders. Quinidine induced a release of calcium by turtle liver mitochondria. Quinidine inhibited Na transport by increasing the resistance of the active pathway to Na transport without affecting the electromotive force. Amphotericin B addition to the mucosal solution partially reversed the inhibitory effect of quinidine on Na transport, thus suggesting that quinidine decreases Na transport by decreasing the permeability of luminal membrane to Na. The effect of amiloride was unaltered in the presence of quinidine. Vasopressin failed to stimulate Na transport in the presence of quinidine, suggesting that the drug interferes with the natriferetic effect in addition to interfering with the hydrosmotic effect. The effect of quinidine was not prevented by inhibition of cyclooxygenase system or mitochondrial inhibition; thus suggesting that alterations in prostaglandin release or mitochondrial function are not involved in the inhibition of Na transport by quinidine.

CONTROLLED TERM: Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.  
Amiloride: PD, pharmacology  
Amphotericin B: PD, pharmacology  
**\*Bladder: DE, drug effects**  
Bufo marinus  
Calcium: ME, metabolism  
**Drug Interactions**  
**\*Ion Channels: DE, drug effects**  
Mitochondria, Liver: DE, drug effects  
**\*Quinidine: PD, pharmacology**  
**\*Sodium: ME, metabolism**  
Turtles  
CAS REGISTRY NO.: 1397-89-3 (Amphotericin B); 2609-46-3 (Amiloride); 56-54-2 (Quinidine); 7440-23-5 (Sodium); 7440-70-2 (Calcium)  
CHEMICAL NAME: 0 (Ion Channels)

L146 ANSWER 23 OF 35 MEDLINE  
ACCESSION NUMBER: 80216390 MEDLINE  
DOCUMENT NUMBER: 80216390 PubMed ID: 575741  
TITLE: [Action of some drugs on pressure profile of female urethra (author's transl)].  
Wirkung einiger Pharmaka auf das weibliche Urethradruckprofil.  
AUTHOR: Methfessel H D; Methfessel G  
SOURCE: ZENTRALBLATT FUR GYNAKOLOGIE, (1979) 101 (22) 1453-62.  
Journal code: 21820100R. ISSN: 0044-4197.  
PUB. COUNTRY: GERMANY, EAST: German Democratic Republic  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: German  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198008  
ENTRY DATE: Entered STN: 19900315  
Last Updated on STN: 19900315  
Entered Medline: 19800828

## ABSTRACT:

The action of certain drugs upon the urethra of clinically intact women was studied by measurement of the urethral profile. beta-adrenoreceptor stimulating

and blocking agents, such as fenoterol, propanolol, as well as cholinergics, including carbachol and pyridostigmine, failed to exercise any effect on the urethral pressure profile. On the other hand, anticholinergics, such as atropine and N-butylscopolammonium-bromide, diazepam, and chlorpromazine, produced significant decrease in both maximum urethral pressure and maximum urethral closure pressure. N-butylscopolammonium-bromide and chlorpromazine also shortened the functional length of urethra. Drop of all parameters relating to the urethral pressure profile was observed to take place in response to application of succinylcholine. Phentolamine, an alpha-adrenoreceptor blocking agent, then was administered and caused further reduction of those parameters. The pressure values were elevated by ketamine. The above findings are discussed and compared to present concepts published in literature on medicamentous control of urethral function.

CONTROLLED TERM: Check Tags: Female; Human; Male

Adolescent

Adult

**Butylscopolammonium Bromide: PD, pharmacology**

Chlorpromazine: PD, pharmacology

Diazepam: PD, pharmacology

**Drug Synergism**

English Abstract

Ketamine: PD, pharmacology

Parasympatholytics: PD, pharmacology

**Phentolamine: PD, pharmacology**

Pressure

Succinylcholine: PD, pharmacology

**\*Urethra: DE, drug effects**

CAS REGISTRY NO.: 149-64-4 (Butylscopolammonium Bromide); 306-40-1  
(Succinylcholine); 439-14-5 (Diazepam); 50-53-3  
(Chlorpromazine); 50-60-2 (Phentolamine); 6740-88-1  
(Ketamine)

CHEMICAL NAME: 0 (Parasympatholytics)

L146 ANSWER 24 OF 35 MEDLINE

ACCESSION NUMBER: 76014373 MEDLINE

DOCUMENT NUMBER: 76014373 PubMed ID: 1167189

TITLE: Effects of phenoxybenzamine hydrochloride on canine lower urinary tract: clinical implications.

AUTHOR: Khanna O P; Gonick P

SOURCE: UROLOGY, (1975 Sep) 6 (3) 323-30.  
Journal code: 0366151. ISSN: 0090-4295.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 197511

ENTRY DATE: Entered STN: 19900313

Last Updated on STN: 19900313

Entered Medline: 19751120

#### ABSTRACT:

The results of our study show that phenoxybenzamine hydrochloride, a potent long-acting alpha-adrenergic blocker, has clearly demonstrable effects on urethral function. In a dose of 0.5 mg. per kilogram of body weight it caused a significant lowering of the resting urethral pressure, a decrease in the arterial pressure, and no change in the intravesical pressure. Higher doses caused similar but more pronounced and prolonged effects. The combined use of phenoxybenzamine and bethanechol increased the intravesical pressure and decreased the urethral pressure. It appears that the predominant mechanism of urethral resistance is alpha-adrenergic activity in smooth muscle. A review of the medical literature, our experimental studies, and limited clinical application lead us to conclude that phenoxybenzamine could be useful in treating neurogenic vesical dysfunction of various types, urethral syndrome, urgency incontinence, functional outlet obstruction with or without

vesicoureteral reflux, drug-related obstructive urinary symptoms, partial prostatic obstruction, and ureteral colic. The combination of phenoxybenzamine and bethanechol could be used in managing patients with atony of the bladder of neuropathic or myopathic origin.

CONTROLLED TERM: Check Tags: Animal; Female; Human; Male  
Adult

**Atropine: PD, pharmacology**

Bethanechol Compounds: PD, pharmacology

Bethanechol Compounds: TU, therapeutic use

**\*Bladder: DE, drug effects**

Bladder, Neurogenic: DT, drug therapy

Blood Pressure: DE, drug effects

Dogs

**Drug Interactions**

**Drug Therapy, Combination**

Middle Age

**Phenoxybenzamine: AD, administration & dosage**

**\*Phenoxybenzamine: PD, pharmacology**

**Phenoxybenzamine: TU, therapeutic use**

Pressure

**\*Urethra: DE, drug effects**

**Urethra: PH, physiology**

Urethral Diseases: DT, drug therapy

Urinary Incontinence, Stress: DT, drug therapy

CAS REGISTRY NO.: 51-55-8 (Atropine); 59-96-1 (Phenoxybenzamine)

CHEMICAL NAME: 0 (Bethanechol Compounds)

L146 ANSWER 25 OF 35 MEDLINE

ACCESSION NUMBER: 72051037 MEDLINE

DOCUMENT NUMBER: 72051037 PubMed ID: 4107866

TITLE: The reactivity of isolated urinary bladder strips of the guinea-pig towards electric stimulation.

AUTHOR: De Sy W

SOURCE: ARCHIVES INTERNATIONALES DE PHYSIOLOGIE ET DE BIOCHIMIE,  
(1971 Aug) 79 (3) 459-68.

Journal code: 0405355. ISSN: 0003-9799.

PUB. COUNTRY: Belgium

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 197202

ENTRY DATE: Entered STN: 19900310

Last Updated on STN: 19900310

Entered Medline: 19720202

CONTROLLED TERM: Check Tags: Animal; Female; In Vitro; Male

Acetylcholine: AI, antagonists & inhibitors

**Atropine: PD, pharmacology**

**Bladder: DE, drug effects**

**\*Bladder: PH, physiology**

Depression, Chemical

**Drug Antagonism**

**\*Electric Stimulation**

Guinea Pigs

Isoproterenol: PD, pharmacology

Methonium Compounds: PD, pharmacology

Muscle, Smooth: PH, physiology

Norepinephrine: PD, pharmacology

**Phentolamine: PD, pharmacology**

Propranolol: PD, pharmacology

Receptors, Adrenergic

Stimulation, Chemical

CAS REGISTRY NO.: 50-60-2 (Phentolamine); 51-41-2 (Norepinephrine); 51-55-8  
(Atropine); 51-84-3 (Acetylcholine); 525-66-6

CHEMICAL NAME: (Propranolol); 7683-59-2 (Isoproterenol)  
0 (Methonium Compounds); 0 (Receptors, Adrenergic)

L146 ANSWER 26 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 2002437700 EMBASE  
TITLE: Female stress and urge incontinence in family practice:  
Insight into the lower urinary tract.  
AUTHOR: Viktrup L.  
CORPORATE SOURCE: Dr. L. Viktrup, Eli Lilly and Company, Faris II, Drop Code  
6112, Indianapolis, IN 46285, Denmark  
SOURCE: International Journal of Clinical Practice, (2002) 56/9  
(694-700).  
Refs: 84  
ISSN: 1368-5031 CODEN: IJCPF  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
010 Obstetrics and Gynecology  
017 Public Health, Social Medicine and Epidemiology  
028 Urology and Nephrology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

As many as 25% of all women are affected by urinary incontinence, but only a few are treated. This frequent, often medically unrecognised, condition occurs in women of all ages. The continence mechanism is based on bladder detrusor control, intact anatomical structures in and around the urethra, correct positioning of the bladder neck and a comprehensive innervation of the lower urinary tract. Age and childbearing are established risk factors for the development of urinary incontinence, but other factors are currently suggested. The evaluation of urinary incontinence should include history, gynaecological examination, urine test, frequency-volume diary and a pad-weighting test. Female urinary incontinence can be treated in general practice by simple means, e.g. pelvic floor muscle training, bladder training, electrostimulation, drug therapy, or a combination of these approaches. This review updates the knowledge of the continence mechanism and summarises the epidemiology, risk factors, assessment and treatment of urinary incontinence in general practice.

CONTROLLED TERM:

Medical Descriptors:

- \*stress incontinence: DI, diagnosis
- \*stress incontinence: DT, drug therapy
- \*stress incontinence: EP, epidemiology
- \*stress incontinence: ET, etiology
- \*stress incontinence: SI, side effect
- \*stress incontinence: SU, surgery
- \*stress incontinence: TH, therapy
- \*urge incontinence: DI, diagnosis
- \*urge incontinence: DT, drug therapy
- \*urge incontinence: EP, epidemiology
- \*urge incontinence: ET, etiology
- \*urge incontinence: SI, side effect
- \*urge incontinence: SU, surgery
- \*urge incontinence: TH, therapy
- general practice
- urethra
- detrusor muscle
- bladder neck
- innervation
- age
- pregnancy
- risk factor

anamnesis  
gynecological examination  
urinalysis  
urinary frequency  
urine volume  
diagnostic test  
pelvis floor  
muscle training  
electrostimulation therapy  
medical assessment  
central nervous system function  
peripheral nervous system function  
autonomic nervous system function

**micturition**

delivery  
menopause  
obesity  
constipation  
pelvic disease  
pelvis surgery  
neurologic disease  
chronic obstructive lung disease  
functional disease  
human  
female  
controlled study  
review  
priority journal

**Drug Descriptors:**

**alpha adrenergic receptor blocking agent: AE, adverse drug reaction**

diuretic agent: AE, adverse drug reaction

estrogen: DT, drug therapy

cholinergic receptor blocking agent: AE, adverse drug reaction

cholinergic receptor blocking agent: DT, drug therapy

**serotonin uptake inhibitor: CB, drug combination**

serotonin uptake inhibitor: DT, drug therapy

serotonin uptake inhibitor: PD, pharmacology

**noradrenalin uptake inhibitor: CB, drug combination**

noradrenalin uptake inhibitor: DT, drug therapy

noradrenalin uptake inhibitor: PD, pharmacology

**tolterodine: AE, adverse drug reaction**

**tolterodine: DT, drug therapy**

propantheline bromide: AE, adverse drug reaction

propantheline bromide: DT, drug therapy

**darifenacin: AE, adverse drug reaction**

**darifenacin: DT, drug therapy**

**oxybutynin: AE, adverse drug reaction**

**oxybutynin: DT, drug therapy**

tricyclic antidepressant agent: AE, adverse drug reaction

tricyclic antidepressant agent: DT, drug therapy

imipramine: AE, adverse drug reaction

imipramine: DT, drug therapy

duloxetine: DT, drug therapy

duloxetine: PD, pharmacology

placebo

CAS REGISTRY NO.: (tolterodine) 124937-51-5; (propantheline bromide) 298-50-0, 50-34-0; (darifenacin) 133099-04-4, 133099-07-7; (oxybutynin) 1508-65-2, 5633-20-5; (imipramine) 113-52-0, 50-49-7; (duloxetine) 116539-59-4, 136434-34-9

L146 ANSWER 27 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2003149857 EMBASE

TITLE: Management of incontinence in the elderly.

AUTHOR: Reznicek S.B.

CORPORATE SOURCE: S.B. Reznicek, 1011 Sunnyside Dr., Cadillac, MI 49601,  
United States. rez@netonecom.net

SOURCE: Journal of Gender-Specific Medicine, (2002) 5/5 (43-48).  
Refs: 7

ISSN: 1523-7036 CODEN: JGMOA7

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology  
020 Gerontology and Geriatrics  
028 Urology and Nephrology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

Urinary incontinence in the elderly will continue to grow as a health and lifestyle issue as this population expands. Additionally, as older Americans seek to remain active in their careers and recreational pursuits, they are likely to be more intensive in seeking consultation for this condition. Evaluation of incontinence has become simpler and more focused to allow for an earlier and more precise diagnosis, which in turn expedites therapy. In the past, surgery was often thought of as the sole modality, which likely prevented larger numbers of patients from seeking relief. Today, more conservative treatments tend to bring more patient referrals to physicians' offices. Incontinence affects 15-30% of older patients living at home, one-third of those in acute care hospitals, and half of those in nursing homes. It is responsible in part for up to half of all nursing home admissions. Because of the diagnostic and therapeutic variability between men and women, a gender-specific discussion is called for. Catheter care is sufficiently challenging so as to merit a specific tutorial.

CONTROLLED TERM: Medical Descriptors:

- \*urine incontinence: DI, diagnosis
- \*urine incontinence: DT, drug therapy
- \*urine incontinence: ET, etiology
- \*urine incontinence: SU, surgery
- \*urine incontinence: TH, therapy
- aged
- daily life activity
- career
- recreation
- diagnostic accuracy
- conservative treatment
- patient referral
- primary medical care
- nursing home
- sex difference
- catheterization
- pathophysiology
- stress incontinence: DT, drug therapy
- stress incontinence: SI, side effect
- stress incontinence: TH, therapy
- urine retention: SI, side effect
- kinesiotherapy
- xerostomia: SI, side effect
- confusion: SI, side effect
- drowsiness: SI, side effect
- central nervous system disease: SI, side effect

urethra surgery

**prostate hypertrophy: DT, drug therapy**

skin disease: CO, complication

skin disease: TH, therapy

antiinflammatory activity

antifungal activity

dermatitis: CO, complication

dermatitis: DT, drug therapy

dermatitis: PC, prevention

bladder spasm: DT, drug therapy

urinary tract infection: CO, complication

urinary tract infection: DT, drug therapy

urinary tract infection: PC, prevention

human

review

Drug Descriptors:

diuretic agent

neuroleptic agent

antidepressant agent

antiparkinson agent

**alpha adrenergic receptor blocking agent: AE, adverse drug reaction**

dipeptidyl carboxypeptidase inhibitor: AE, adverse drug reaction

narcotic agent: AE, adverse drug reaction

alcohol: TO, drug toxicity

sedative agent: AE, adverse drug reaction

estrogen: DT, drug therapy

cholinergic receptor blocking agent: AE, adverse drug reaction

cholinergic receptor blocking agent: DO, drug dose

cholinergic receptor blocking agent: DT, drug therapy

collagen: DT, drug therapy

collagen: UR, intraurethral drug administration

**oxybutynin: DO, drug dose**

**oxybutynin: DT, drug therapy**

**tolterodine: DO, drug dose**

**tolterodine: DT, drug therapy**

hyoscyamine: DO, drug dose

hyoscyamine: DT, drug therapy

propantheline bromide: DO, drug dose

propantheline bromide: DT, drug therapy

tamsulosin: DO, drug dose

tamsulosin: DT, drug therapy

**terazosin: DO, drug dose**

**terazosin: DT, drug therapy**

**doxazosin: DO, drug dose**

**doxazosin: DT, drug therapy**

**prazosin: DO, drug dose**

**prazosin: DT, drug therapy**

**nystatin: CB, drug combination**

nystatin: PD, pharmacology

**triamcinolone acetonide: CB, drug combination**

triamcinolone acetonide: PD, pharmacology

ascorbic acid: DO, drug dose

ascorbic acid: PO, oral drug administration

acetic acid: DT, drug therapy

nitrofurantoin: DT, drug therapy

quinoline derived antiinfective agent: DT, drug therapy

gentamicin: DO, drug dose

gentamicin: DT, drug therapy

sodium chloride

antibiotic agent: DT, drug therapy

CAS REGISTRY NO.: unindexed drug  
(alcohol) 64-17-5; (collagen) 9007-34-5; (oxybutynin)  
**1508-65-2, 5633-20-5**; (tolterodine)  
**124937-51-5**; (hyoscyamine) 101-31-5, 306-03-6;  
(propantheline bromide) 298-50-0, 50-34-0; (tamsulosin)  
106133-20-4, 106138-88-9, 106463-17-6, 80223-99-0,  
94666-07-6; (terazosin) **63074-08-8**,  
**63590-64-7**; (doxazosin) **74191-85-8**;  
(prazosin) **19216-56-9, 19237-84-4**;  
(nystatin) 1400-61-9, 34786-70-4, 62997-67-5;  
(triamcinolone acetone) 76-25-5; (ascorbic acid)  
134-03-2, 15421-15-5, 50-81-7; (acetic acid) 127-08-2,  
127-09-3, 64-19-7, 71-50-1; (nitrofurantoin) 54-87-5,  
67-20-9; (gentamicin) 1392-48-9, 1403-66-3, 1405-41-0;  
(sodium chloride) 7647-14-5

L146 ANSWER 28 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001133800 EMBASE  
TITLE: Effect of temperature on guinea pig urinary bladder  
contraction mediated via P2X-receptors.  
AUTHOR: Ziganshin A.U.; Rychkov A.V.; Ziganshina L.E.  
CORPORATE SOURCE: A.U. Ziganshin, Department of Pharmacology, Kazan State  
Medical University, Kazan, Russian Federation  
SOURCE: Bulletin of Experimental Biology and Medicine, (2001)  
130/10 (961-963).

Refs: 14  
ISSN: 0007-4888 CODEN: BEXBAN

COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 029 Clinical Biochemistry  
037 Drug Literature Index  
030 Pharmacology  
002 Physiology  
028 Urology and Nephrology

LANGUAGE: English  
SUMMARY LANGUAGE: English

ABSTRACT:  
In vitro experiments showed that P2X-receptor agonist .alpha.,.beta.-methylene-ATP and electrical field stimulation in the presence of muscarinic and .alpha.-adrenoreceptors blockers induced contractile responses of isolated guinea pig bladder, which were more pronounced at 30.degree.C than at 37.degree.C or 42.degree.C. P2X-receptor antagonist pyridoxal-6-phosphate-2',4'-disulfonic acid, produced a more potent inhibitory effect on contractions induced by electrical field stimulation at 30.degree.C in comparison with that at 37.degree.C or 42.degree.C, while the contractions induced by .alpha.,.beta.-methylene-ATP were similarly suppressed at all examined temperatures.

CONTROLLED TERM: Medical Descriptors:  
\*temperature dependence  
\*bladder contraction  
nonhuman  
animal tissue  
animal experiment  
guinea pig  
in vitro study  
electrostimulation  
drug inhibition  
drug potency  
drug effect  
bladder  
article  
Drug Descriptors:

\*purine P2X receptor: EC, endogenous compound  
purinergic receptor stimulating agent: PD, pharmacology  
purinergic receptor stimulating agent: CM, drug comparison  
alpha,beta methyleneadenosine triphosphate: PD,  
pharmacology  
alpha,beta methyleneadenosine triphosphate: CM, drug  
comparison  
muscarinic receptor blocking agent: PD,  
pharmacology  
alpha adrenergic receptor blocking agent: PD,  
pharmacology  
purinergic receptor blocking agent: PD, pharmacology  
purinergic receptor blocking agent: CM, drug comparison  
pyridoxal phosphate 6 azophenyl 2',4' disulfonic acid: PD,  
pharmacology  
pyridoxal phosphate 6 azophenyl 2',4' disulfonic acid: CM,  
drug comparison  
atropine: PD, pharmacology  
phentolamine: PD, pharmacology  
CAS REGISTRY NO.: (alpha,beta methyleneadenosine triphosphate) 7292-42-4;  
(pyridoxal phosphate 6 azophenyl 2',4' disulfonic acid)  
149017-66-3; (atropine) 51-55-8, 55-48-1; (phentolamine)  
50-60-2, 73-05-2

L146 ANSWER 29 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 97020195 EMBASE  
DOCUMENT NUMBER: 1997020195  
TITLE: [Drugs for micturition disorders in the elderly].  
MEDIKAMENTE BEI MIKTIONSSTORUNGEN IM ALTER.  
AUTHOR: Schultz-Lampel D.; Thuroff J.W.  
CORPORATE SOURCE: Dr. D. Schultz-Lampel, Klinik fur Urologie/Kinderurologie,  
Klinikum Wuppertal GmbH, Universitat Witten/Herdekke,  
Heusnerstrasse 40, D-42283 Wuppertal, Germany  
SOURCE: Urologe - Ausgabe B, (1996) 36/6 (444-448).  
Refs: 18  
ISSN: 0042-1111 CODEN: URLBBQ  
COUNTRY: Germany  
DOCUMENT TYPE: Journal; (Short Survey)  
FILE SEGMENT: 020 Gerontology and Geriatrics  
028 Urology and Nephrology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: German  
SUMMARY LANGUAGE: German  
CONTROLLED TERM: Medical Descriptors:  
\*micturition disorder: DT, drug therapy  
\*stress incontinence: DT, drug therapy  
constipation: SI, side effect  
hallucination: SI, side effect  
human  
muscle cramp: SI, side effect  
mydriasis: SI, side effect  
nausea: SI, side effect  
senescence  
short survey  
tachycardia: SI, side effect  
xerostomia: SI, side effect  
Drug Descriptors:  
beta 2 adrenergic receptor stimulating agent: DT, drug  
therapy  
bethanechol: DT, drug therapy  
carbachol: DT, drug therapy

cholinergic receptor blocking agent: DT, drug therapy  
cholinergic receptor blocking agent: AE, adverse drug  
reaction

clenbuterol: DT, drug therapy

diclofenac: DT, drug therapy

distigmine: DT, drug therapy

distigmine bromide

emepronium: DT, drug therapy

emepronium bromide

estriol: DT, drug therapy

estrogen: DT, drug therapy

**estrogen: CB, drug combination**

flavoxate: DT, drug therapy

flurbiprofen: DT, drug therapy

gestagen: DT, drug therapy

**gestagen: CB, drug combination**

imipramine: DT, drug therapy

indometacin: DT, drug therapy

isoprenaline: DT, drug therapy

**oxybutynin: DT, drug therapy**

propantheline bromide: DT, drug therapy

propiverine: DT, drug therapy

prostaglandin synthase inhibitor: DT, drug therapy

salbutamol: DT, drug therapy

spasmolytic agent: DT, drug therapy

**terazosin**

terbutaline: DT, drug therapy

tricyclic antidepressant agent: DT, drug therapy

trospium chloride

unindexed drug

CAS REGISTRY NO.:

(bethanechol) 590-63-6, 674-38-4, 91609-06-2; (carbachol)  
462-58-8, 51-83-2; (clenbuterol) 21898-19-1, 37148-27-9;  
(diclofenac) 15307-79-6, 15307-86-5; (distigmine)  
17299-00-2; (distigmine bromide) 15876-67-2; (emepronium)  
27892-33-7; (emepronium bromide) 3614-30-0; (estriol)  
50-27-1; (flavoxate) 15301-69-6, 3717-88-2; (flurbiprofen)  
5104-49-4; (imipramine) 113-52-0, 50-49-7; (indometacin)  
53-86-1, 74252-25-8, 7681-54-1; (isoprenaline) 299-95-6,  
51-30-9, 6700-39-6, 7683-59-2; (oxybutynin)  
**1508-65-2, 5633-20-5;** (propantheline  
bromide) 298-50-0, 50-34-0; (propiverine) 60569-19-9;  
(salbutamol) 18559-94-9; (terazosin) **63074-08-8,**  
**63590-64-7;** (terbutaline) 23031-25-6; (trospium  
chloride) 10405-02-4.

CHEMICAL NAME:

Dridase; Mictonorm; Uroripirin; Spasmex; Spasuret;  
Bricanyl; Spiropent; Tofranil; Amuno; Froben; Voltaren;  
Flotrin; Myocholine; Ubretid

L146 ANSWER 30 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 95188724 EMBASE

DOCUMENT NUMBER: 1995188724

TITLE: Recent progress in the pharmacotherapy of diseases of the  
lower urinary tract.

AUTHOR: Hieble J.P.; McCafferty G.P.; Naselsky D.P.; Bergsma D.J.;  
Ruffolo Jr. R.R.

CORPORATE SOURCE: Pharmacological Sciences, SmithKline Beecham  
Pharmaceuticals, P.O.Box 1539, King of Prussia, PA 19406,  
United States

SOURCE: European Journal of Medicinal Chemistry, (1995) 30/SUPPL.  
(269s-298s).

ISSN: 0223-5234 CODEN: EJMCA5

COUNTRY: France

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 008 Neurology and Neurosurgery  
028 Urology and Nephrology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:  
\*prostate hypertrophy: SU, surgery  
\*prostate hypertrophy: DT, drug therapy  
\*urine incontinence  
animal model  
animal tissue  
conference paper  
controlled study  
dog  
guinea pig  
human  
intravenous drug administration  
nonhuman  
rat  
torsade des pointes  
xerostomia  
Drug Descriptors:  
\*adrenergic receptor stimulating agent: DT, drug therapy  
\*alpha adrenergic receptor blocking agent: DT, drug therapy  
therapy  
\*potassium channel affecting agent: DT, drug therapy  
\*steroid 5alpha reductase inhibitor: DT, drug therapy  
alfuzosin: DT, drug therapy  
tamsulosin: DT, drug therapy  
cromakalim: DT, drug therapy  
emepronium: DT, drug therapy  
epristeride: DT, drug therapy  
finasteride: DT, drug therapy  
flutamide: DT, drug therapy  
furosemide: DT, drug therapy  
midodrine: DT, drug therapy  
midodrine: CB, drug combination  
mk 0963: DT, drug therapy  
muscarinic receptor blocking agent: DT, drug therapy  
therapy  
muscarinic receptor blocking agent: AE, adverse drug reaction  
naftopidil: DT, drug therapy  
otenzepad: DT, drug therapy  
oxybutynin: DT, drug therapy  
pinacidil: DT, drug therapy  
prazosin: DT, drug therapy  
propantheline bromide: DT, drug therapy  
8 [3 [4 (2 methoxyphenyl) 1 piperazinyl]propylcarbamoyl] 3  
methylflavone: DT, drug therapy  
sl 890591: DT, drug therapy  
tachykinin receptor antagonist: DT, drug therapy  
terazosin: CB, drug combination  
terazosin: DT, drug therapy  
terodiline: AE, adverse drug reaction  
terodiline: DT, drug therapy  
turosteride: DT, drug therapy  
unindexed drug  
unclassified drug

CAS REGISTRY NO.: (alfuzosin) 81403-80-7; (tamsulosin) 80223-99-0;  
(cromakalim) 94470-67-4; (emepronium) 27892-33-7;

(epristeride) 119169-78-7; (finasteride) 98319-26-7;  
(flutamide) 13311-84-7; (furosemide) 54-31-9; (midodrine)  
3092-17-9, 42794-76-3; (naftopidil) 57149-07-2; (otenzepad)  
100158-38-1, 102394-31-0; (oxybutynin) 1508-65-2,  
5633-20-5; (pinacidil) 60560-33-0; (prazosin)  
19216-56-9, 19237-84-4; (propantheline  
bromide) 298-50-0, 50-34-0; (8 [3 [4 (2 methoxyphenyl) 1  
piperazinyl]propylcarbamoyl] 3 methylflavone) 152735-23-4;  
(terazosin) 63074-08-8, 63590-64-7;  
(terodiline) 15793-40-5, 7082-21-5; (turosteride)  
137099-09-3

CHEMICAL NAME: Sb 216469; Mk 0963; Sl 890591

L146 ANSWER 31 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 92348791 EMBASE

DOCUMENT NUMBER: 1992348791

TITLE: [Urological pathology in the elderly].  
PATOLOGIA UROLOGICA EN EL ANCIANO.

AUTHOR: Cots Yago J.M.

CORPORATE SOURCE: ABS Dr. Carles Ribas, Barcelona, Spain

SOURCE: Atencion Primaria, (1992) 10/6 (837-838+840-842).

ISSN: 0212-6567 CODEN: ATEPEY

COUNTRY: Spain

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 005 General Pathology and Pathological Anatomy

020 Gerontology and Geriatrics

028 Urology and Nephrology

037 Drug Literature Index

LANGUAGE: Spanish

CONTROLLED TERM: Medical Descriptors:

\*prostate hypertrophy: DT, drug therapy

\*prostate hypertrophy: SU, surgery

\*urinary tract infection: DT, drug therapy

\*urine incontinence: DT, drug therapy

aged

female

human

male

review

Drug Descriptors:

\*antibiotic agent: DT, drug therapy

\*imipramine: DT, drug therapy

\*oxybutynin: DT, drug therapy

\*prazosin: DT, drug therapy

\*propantheline bromide: DT, drug therapy

\*terazosin: DT, drug therapy

amoxicillin: DT, drug therapy

amoxicillin: CB, drug combination

cefonicid: DT, drug therapy

clavulanic acid: DT, drug therapy

clavulanic acid: CB, drug combination

norfloxacin: DT, drug therapy

pipemidic acid: DT, drug therapy

CAS REGISTRY NO.: (imipramine) 113-52-0, 50-49-7; (oxybutynin)

1508-65-2, 5633-20-5; (prazosin)

19216-56-9, 19237-84-4; (propantheline

bromide) 298-50-0, 50-34-0; (terazosin) 63074-08-8

, 63590-64-7; (amoxicillin) 26787-78-0,

61336-70-7; (cefonicid) 61270-58-4, 61270-78-8; (clavulanic

acid) 58001-44-8; (norfloxacin) 70458-96-7; (pipemidic

acid) 51940-44-4

L146 ANSWER 32 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 92030436 EMBASE

DOCUMENT NUMBER: 1992030436

TITLE: Benign and malignant prostatic diseases.

AUTHOR: Crawford E.D.

CORPORATE SOURCE: University of Colorado Health Sciences Center, Denver, CO,  
United States

SOURCE: American Family Physician, (1991) 44/5 SUPPL. (65S-70S).

ISSN: 0002-838X CODEN: AFPYAE

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer  
020 Gerontology and Geriatrics  
028 Urology and Nephrology  
030 Pharmacology  
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT:

The risk of prostatic diseases and disorders increases with age. Symptomatic benign prostatic hyperplasia is often treated with transurethral resection of the prostate. Antibiotic therapy is generally effective in bacterial prostatitis, but both chronic bacterial prostatitis with recurrent urinary tract infection and nonbacterial prostatitis remain difficult to treat. Early diagnosis of prostate cancer improves survival. Therapeutic options include surgery, radiotherapy and hormone therapy.

CONTROLLED TERM: Medical Descriptors:

\*prostate cancer: DI, diagnosis

\*prostate cancer: DT, drug therapy

**\*prostate hypertrophy: DI, diagnosis**

**\*prostate hypertrophy: TH, therapy**

\*prostatitis: DI, diagnosis

\*prostatitis: ET, etiology

\*prostatitis: TH, therapy

adult

human

male

priority journal

review

Drug Descriptors:

\*antibiotic agent: DT, drug therapy

\*estrogen: DT, drug therapy

\*goserelin: DT, drug therapy

\*leuporelin: DT, drug therapy

\*nonsteroid antiinflammatory agent: DT, drug therapy

**\*oxybutynin: DT, drug therapy**

**alpha adrenergic receptor blocking agent: DT, drug therapy**

carbenicillin: DT, drug therapy

carindacillin

cefalexin: DT, drug therapy

ciprofloxacin: DT, drug therapy

cotrimoxazole: DT, drug therapy

**diazepam: CB, drug combination**

diazepam: DT, drug therapy

doxycycline

erythromycin: DT, drug therapy

ofloxacin: DT, drug therapy

minocycline: DT, drug therapy

norfloxacin: DT, drug therapy

**prazosin: DT, drug therapy**

**prazosin: CB, drug combination**

**sulfamethoxazole: CB, drug combination**  
sulfamethoxazole: DT, drug therapy  
**trimethoprim: CB, drug combination**  
trimethoprim: DT, drug therapy  
CAS REGISTRY NO.: (goserelin) 65807-02-5; (leuprorelin) 53714-56-0,  
74381-53-6; (oxybutynin) **1508-65-2**,  
**5633-20-5**; (carbenicillin) 17230-86-3, 4697-36-3,  
4800-94-6; (carindacillin) 26605-69-6, 35531-88-5;  
(cefalexin) 15686-71-2, 23325-78-2; (ciprofloxacin)  
85721-33-1; (cotrimoxazole) 8064-90-2; (diazepam) 439-14-5;  
(doxycycline) 10592-13-9, 17086-28-1, 564-25-0;  
(erythromycin) 114-07-8, 70536-18-4; (ofloxacin)  
82419-36-1; (minocycline) 10118-90-8, 11006-27-2,  
13614-98-7; (norfloxacin) 70458-96-7; (prazosin)  
**19216-56-9, 19237-84-4**;  
(sulfamethoxazole) 723-46-6; (trimethoprim) 738-70-5  
CHEMICAL NAME: Bactrim; Septra; Geocillin; Minocin; Noroxin;  
Cipro; Floxin; Ditropan; Minipress; Lupron; Zoladex

L146 ANSWER 33 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 88234769 EMBASE  
DOCUMENT NUMBER: 1988234769  
TITLE: A review of flavoxate hydrochloride in the treatment of  
urge incontinence.  
AUTHOR: Ruffmann R.  
CORPORATE SOURCE: Medical Department, Recordati SpA, 20148 Milan, Italy  
SOURCE: Journal of International Medical Research, (1988) 16/5  
(317-330).  
ISSN: 0300-0605 CODEN: JIMRBV  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 028 Urology and Nephrology  
052 Toxicology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English

ABSTRACT:  
This article provides a review of the use of flavoxate hydrochloride in the treatment of urge incontinence. It outlines the pharmacology, mode of action, toxicology and pharmacokinetic studies which have been carried out, and then reviews the clinical studies, including those involving patients with benign prostatic hypertrophy. The effects of dosages of 600-1200 mg/day are compared, particularly regarding safety and tolerability factors. Finally, alternative therapies to flavoxate hydrochloride (.alpha.-adrenergic receptor blockers, oxybutinin chloride, terodiline hydrochloride, emepronium bromide and imipramine) are summarized. The article is written in the knowledge of recent evidence which indicates that flavoxate hydrochloride exhibits only weak anticholinergic activity on receptors involved in the control of the lower urinary tract.

CONTROLLED TERM: Medical Descriptors:  
**\*prostate hypertrophy**  
\*urge incontinence: DT, drug therapy  
anticholinergic effect  
depression: SI, side effect  
drug mechanism  
edema: SI, side effect  
headache: SI, side effect  
heartburn: SI, side effect  
pharmacodynamics  
rash: SI, side effect

toxicity testing  
vertigo: SI, side effect  
xerostomia: SI, side effect  
psychological aspect  
review  
human  
priority journal  
side effect  
Drug Descriptors:  
\*flavoxate: TO, drug toxicity  
    **\*flavoxate: CB, drug combination**  
\*flavoxate: CM, drug comparison  
\*flavoxate: DO, drug dose  
\*flavoxate: DT, drug therapy  
\*flavoxate: PK, pharmacokinetics  
\*flavoxate: PD, pharmacology  
\*flavoxate: AE, adverse drug reaction  
emepronium  
imipramine  
nicergoline  
    **oxybutynin**  
phenoxybenzamine  
phéntolamine  
    **prazosin**  
terodiline

CAS REGISTRY NO.: (flavoxate) 15301-69-6, 3717-88-2; (emepronium) 27892-33-7;  
(imipramine) 113-52-0, 50-49-7; (nicergoline) 27848-84-6;  
(oxybutynin) **1508-65-2, 5633-20-5**;  
(phenoxybenzamine) 59-96-1, 63-92-3; (phentolamine)  
50-60-2, 73-05-2; (prazosin) **19216-56-9**,  
**19237-84-4**; (terodiline) 15793-40-5, 7082-21-5

L146 ANSWER 34 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 85206589 EMBASE

DOCUMENT NUMBER: 1985206589

TITLE: Characterization of the muscarinic cholinceptors in the  
human detrusor.

AUTHOR: Nilvebrant L.; Andersson K.-E.; Mattiasson A.

CORPORATE SOURCE: Department of Pharmacology, Research and Development,  
KabiVitrum AB, Stockholm, Sweden

SOURCE: Journal of Urology, (1985) 134/2 (418-423).

CODEN: JOURAA

COUNTRY: United States

DOCUMENT TYPE: Journal

FILE SEGMENT: 037 Drug Literature Index  
028 Urology and Nephrology  
030 Pharmacology  
023 Nuclear Medicine

LANGUAGE: English

ABSTRACT:

Contractions of the human detrusor are thought to be mediated mainly via cholinergic muscarinic receptors. In the present study, we used a receptor-binding technique with 1-quinuclidinyl[phenyl 4-3H]benzilate ((-)3H-QNB) as radioligand to directly demonstrate the presence of muscarinic receptors in homogenates of the human detrusor. The binding of (-)3H-QNB was of high affinity ( $K(D) = (1.2 \pm 0.1) \times 10^{-10}$  M), saturable ( $R_0 = 160 \pm 15$  fmol./mg. protein) and possessed the pharmacological specificity expected of an interaction with muscarinic receptors. Muscarinic receptor antagonists were bound to a virtually uniform population of sites, whereas muscarinic receptor agonists recognized more than one population of muscarinic binding sites. The affinities of a series of antimuscarinic drugs, determined in competition experiments with (-)3H-QNB, were found to correlate with the capacity to inhibit carbachol-induced contractions in isolated human bladder muscle.

Binding data together with the functional data indicated that the human detrusor does not contain any significant number of muscarinic spare receptors. The results suggest that a selective effect on the muscarinic receptors of human bladder is not possible to obtain with presently available antimuscarinic agents.

CONTROLLED TERM: Medical Descriptors:  
\*bladder contraction  
\*bladder muscle  
\*drug efficacy  
    \*drug interaction  
\*drug receptor binding  
\*quinuclidinyl benzilate h 3  
\*smooth muscle contraction  
priority journal  
pharmacokinetics  
muscle  
human  
normal human  
autonomic nervous system  
    bladder  
human cell  
Drug Descriptors:  
\*atropine  
\*carbachol  
\*cholinergic receptor blocking agent  
\*diazepam  
\*dicycloverine  
\*emepronium  
\*imipramine  
\*methylatropine  
\*muscarinic receptor  
    \*oxybutynin  
    \*prazosin  
\*propantheline bromide  
\*terbutaline  
\*terodiline  
radioisotope  
CAS REGISTRY NO.: (atropine) 51-55-8, 55-48-1; (carbachol) 462-58-8, 51-83-2;  
(diazepam) 439-14-5; (dicycloverine) 50815-09-3, 67-92-5,  
77-19-0; (emepronium) 27892-33-7; (imipramine) 113-52-0,  
50-49-7; (methylatropine) 31610-87-4; (oxybutynin)  
1508-65-2, 5633-20-5; (prazosin)  
19216-56-9, 19237-84-4; (propantheline  
bromide) 298-50-0, 50-34-0; (terbutaline) 23031-25-6;  
(terodiline) 15793-40-5, 7082-21-5  
COMPANY NAME: Amersham; Marion; Hoffmann la roche; Kabi vitrum; Pfizer;  
Draco  
L146 ANSWER 35 OF 35 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.  
ACCESSION NUMBER: 83242170 EMBASE  
DOCUMENT NUMBER: 1983242170  
TITLE: Differences between binding affinities of some  
antimuscarinic drugs in the parotid gland and those in the  
urinary bladder and ileum.  
AUTHOR: Nilvebrant L.; Sparf B.  
CORPORATE SOURCE: Dep. Pharmacol., KabiVirum AB, S-11287 Stockholm, Sweden  
SOURCE: Acta Pharmacologica et Toxicologica, (1983) 53/4 (304-313).  
CODEN: APTOA6  
COUNTRY: Denmark  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 037 Drug Literature Index  
030 Pharmacology

002      Physiology  
023      Nuclear Medicine  
011      Otorhinolaryngology  
003      Endocrinology

LANGUAGE:      English

ABSTRACT:

Possible differences between the muscarinic receptors in the guinea pig urinary bladder and those in the ileum and the parotid gland were investigated, using a receptor binding technique. The affinities of 18 antimuscarinic drugs were indirectly derived from the ability to inhibit the receptor-specific binding of the radioligand (-)3H-QNB. The Hill coefficients were close to unity which indicated that the drugs were bound to apparently uniform populations of receptors within each tissue. In contrast to traditional muscarinic antagonists, four drugs - namely, oxybutynine, dicyclomine, benzhexol and pirenzepine - bound with a significantly higher affinity in the parotid gland than in the urinary bladder and ileum. A tendency towards reversed selectivity was found for secoverine. Thus, the present results further support the hypothesis that differences in muscarinic receptor between tissues exist, e.g. smooth muscle compared with parotid gland, which can be detected only by certain antimuscarinic drugs.

CONTROLLED TERM:      Medical Descriptors:

**\*drug antagonism**  
    \*drug receptor binding  
    \*guinea pig  
    \*n,n dimethyl 3,3 diphenyl 2 butylamine  
    \*quinuclidinyl benzilate h 3  
    \*sympathetic nerve  
    **bladder**  
    ileum  
    parotid gland  
    mouth  
    small intestine  
    pharmacokinetics  
    autonomic nervous system  
    nonhuman  
    animal cell  
    Drug Descriptors:  
    \*4 aminobutyric acid  
    \*atropine  
    \*cholinergic receptor blocking agent  
    \*diazepam  
    \*dicycloverine  
    \*emepronium  
    \*haloperidol  
    \*hexamethonium  
    \*histamine  
    \*mecamylamine  
    \*metenkephalin  
    \*morphine  
    \*muscarinic receptor  
    \*nicotine  
    **\*oxybutynin**  
    \*physostigmine  
    \*pirenzepine  
    \*practolol  
    **\*prazosin**  
    \*promethazine  
    \*propantheline bromide  
    \*quinidine  
    \*receptor  
    \*scopolamine methyl nitrate  
    \*secoverine

\*terbutaline  
\*terodiline  
\*theophylline  
\*trihexyphenidyl  
\*tubocurarine chloride  
\*yohimbine

## CAS REGISTRY NO.:

(4 aminobutyric acid) 28805-76-7, 56-12-2; (atropine) 51-55-8, 55-48-1; (diazepam) 439-14-5; (dicycloverine) 50815-09-3, 67-92-5, 77-19-0; (emepronium) 27892-33-7; (haloperidol) 52-86-8; (hexamethonium) 60-26-4; (histamine) 51-45-6, 56-92-8, 93443-21-1; (mecamylamine) 60-40-2, 826-39-1; (metenkephalin) 58569-55-4; (morphine) 52-26-6, 57-27-2; (nicotine) 54-11-5; (oxybutynin) 1508-65-2, 5633-20-5; (physostigmine) 57-47-6, 64-47-1; (pirenzepine) 28797-61-7, 29868-97-1; (practolol) 6673-35-4; (prazosin) 19216-56-9, 19237-84-4; (promethazine) 58-33-3, 60-87-7; (propantheline bromide) 298-50-0, 50-34-0; (quinidine) 56-54-2; (scopolamine methyl nitrate) 6106-46-3; (secoverine) 57558-44-8; (terbutaline) 23031-25-6; (terodiline) 15793-40-5, 7082-21-5; (theophylline) 58-55-9, 5967-84-0, 8055-07-0, 8061-56-1, 99007-19-9; (trihexyphenidyl) 144-11-6, 52-49-3; (tubocurarine chloride) 57-94-3, 57-95-4, 8006-51-7; (yohimbine) 146-48-5, 65-19-0

## COMPANY NAME:

Radiochemical centre (United Kingdom); Leo (Sweden); Pharmacia (Sweden); Kabi vitrum (Sweden); Sigma (United States); Hoffmann la roche (Switzerland); Ici (United Kingdom); Merrell (United States); Schuchardt (Germany); Recip (Sweden); Boehringer ingelheim (Germany); Pfizer (United States); Draco (Sweden)

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controlled respiration (n=10; CR). Nonbaroreflex sequences were defined as  $\geq 3$  beats in which SAP and PI of the following beat changed in the opposite direction. CAB reduced the number of nonbaroreflex sequences (19.1 $\pm$ 12.3 versus 88.7 $\pm$ 36.6,  $P < 0.05$ ), as did SB (25.3 $\pm$ 11.7 versus 84.6 $\pm$ 23.9,  $P < 0.001$ ) and atropine (11.2 $\pm$ 6.8 versus 94.1 $\pm$ 32.4,  $P < 0.05$ ). SB concomitantly increased baroreflex sensitivity (1.18 $\pm$ 0.11 versus 0.47 $\pm$ 0.09 ms/mm Hg,  $P < 0.01$ ). SAD and CR did not significantly affect their occurrence. CONCLUSIONS: These results suggest that nonbaroreflex sequences represent the expression of an integrated, neurally mediated, feed-forward type of short-term cardiovascular regulation able to interact dynamically with the feedback mechanisms of baroreflex origin in the control of heart period.

L118 ANSWER 5 OF 73 MEDLINE  
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 TITLE: Synergistic receptor-activated calcium increases in single nonpigmented epithelial cells.  
 AUTHOR: Cilluffo M C; Xia S L; Farahbakhsh N A; Fain G L  
 CORPORATE SOURCE: Department of Physiological Science, University of California, Los Angeles 90095-1527, USA.  
 CONTRACT NUMBER: EY06969 (NEI)  
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AB PURPOSE: To determine whether single nonpigmented ciliary body cells contain the signaling mechanism to produce synergistic drug-activated increases in  $Ca^{2+}$ , or whether these responses are produced cooperatively by interaction among groups of cells. METHODS: Suspensions of single nonpigmented cells were plated onto soft collagen gels. Fura-2 fluorescence ratio imaging was used to examine receptor-evoked changes in intracellular  $Ca^{2+}$  concentration. RESULTS: Nonpigmented cells plated on soft collagen gels retained a rounded shape with membrane evaginations visible on their surface. Application of acetylcholine (10  $\mu$ M) or epinephrine (1  $\mu$ M) each produced small increases in intracellular  $Ca^{2+}$ , but in combination they produced a  $Ca^{2+}$  increase of more than 10-fold. This synergistic  $Ca^{2+}$  increase was a result of activation of muscarinic and  $\alpha$ 2-adrenergic receptors because a specific  $\alpha$ 2-adrenergic agonist could substitute for epinephrine in producing the response. The response could be blocked by a specific  $\alpha$ 2-antagonist and a muscarinic antagonist. An  $\alpha$ 1-agonist could not substitute for epinephrine in producing a synergistic increase nor could the synergism be blocked by  $\alpha$ 1- or  $\beta$ -antagonists. The  $Ca^{2+}$  increase was largely produced by release from internal stores, because the peak amplitude of the response was nearly the same in the external solution containing a low  $Ca^{2+}$  concentration; however, the influx of  $Ca^{2+}$  into the cell was responsible for maintenance of a steady component of the  $Ca^{2+}$  increase during maintained drug stimulation and for refilling the internal stores. CONCLUSIONS: Single nonpigmented cells can produce synergistic increases in  $Ca^{2+}$  on multiple receptor activation, indicating that the mechanism of synergism does not require the interaction of multiple cells. The  $Ca^{2+}$  increase is a result of release from internal stores and  $Ca^{2+}$  entry through an as yet undefined conductance or transport system in the plasma membrane.

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